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ORIGINAL CONTRIBUTIONS

Volume 19 **May, 1952** Number 5

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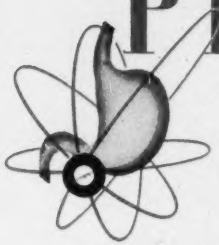

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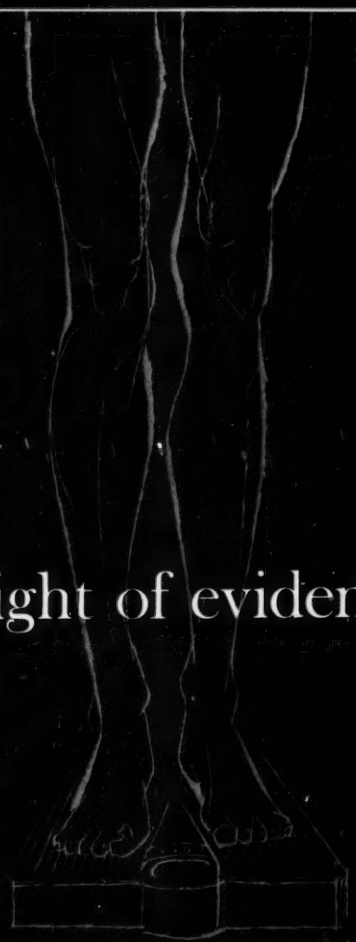

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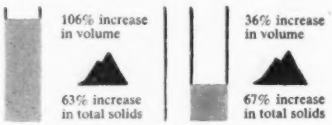

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1. Bralow, S. P., Spellberg, M., Kroll, H., and Necheles, H.: *Am. Jour. Digest Dis.*, 17:119, Apr., 1950.
2. Hardt, L. L., and Steigmann, Frederick: *Am. Jour. Digest. Dis.*, 17:195, June, 1950.

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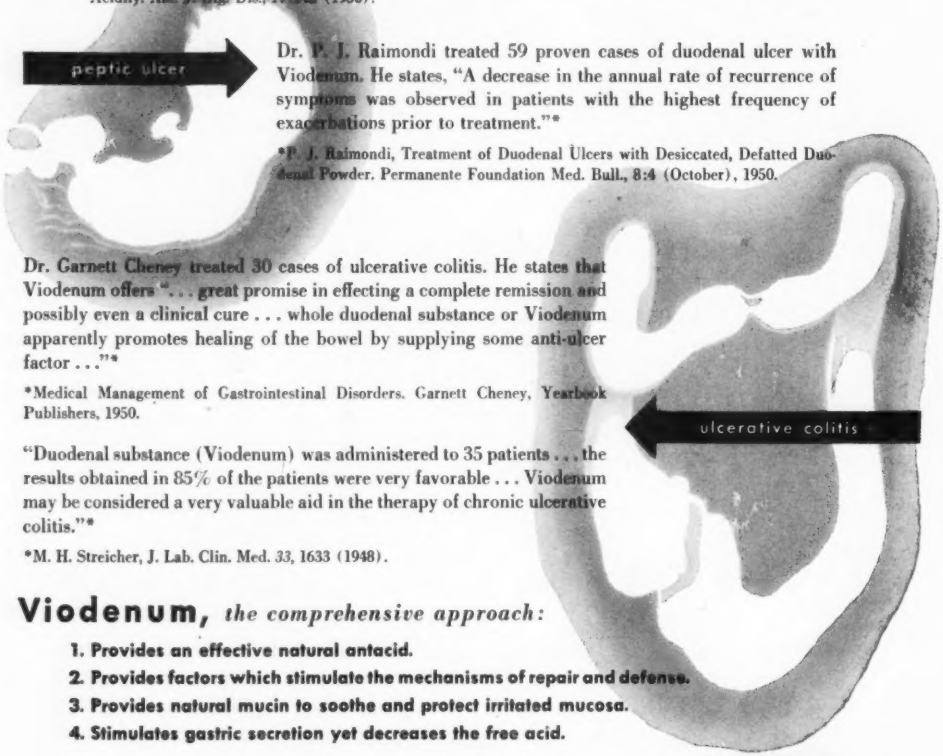

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*P. J. Raimondi, Treatment of Duodenal Ulcers with Desiccated, Defatted Duodenal Powder. Permanente Foundation Med. Bull., 8:4 (October), 1950.

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*Medical Management of Gastrointestinal Disorders. Garnett Cheney, Yearbook Publishers, 1950.

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THE BLOOD PATTERN IN PRE-SYMPTOMATIC MALIGNANCY OF THE GASTROINTESTINAL TRACT

H. LEONARD BOLEN, M. D. Fall River, Massachusetts.

GASTROINTESTINAL malignancy in the pre-symptomatic or latent stage presents a confusing problem in diagnosis, even after a careful clinical evaluation of the patient (1, 2). This is true of malignancy at any site which remains symptomless, but gastric or intestinal cancer has a tendency to remain hidden until wide invasion has occurred, so that by the time the tumor is discovered it is incurable. Welch and Allen (3) deplore the delay before treatment and assert that "theoretically, if all patients were subjected to resection as soon as carcinoma of the stomach developed, all would be cured. . . . The most fruitful method now available to increase the number of cures of cancer of the stomach is to reduce the delay from onset of symptoms to surgical intervention."

An editorial which appeared in 1946 (4) contains some pertinent observations regarding the problem of diagnosis in pre-symptomatic cancer:

"These methods attack the problem of symptomatic cancer—they leave untouched the important field of presymptomatic cancer, or cancer which is as yet symptomless, silent, latent or preclinical. Apparently some cancers are asymptomatic until they are incurable by methods of treatment now available."

"Among the commoner types of cancer that may be silent until they are incurable are some of those that arise in the stomach. . . . Some simple test with which the entire population could be periodically screened is highly desirable. Such tests for detecting tumors should be as simple as those for spyhilis. . . . It is not unreasonable to believe that a simple method for detecting presymptomatic cancer cases will yet be discovered by an intensified and concerted effort."

The magnitude of the problem is a challenge to investigators and any laboratory test which will furnish a clue to discovering potential cancer bearers is of major interest to both internist and surgeon (5).

Many of the tests for cancer have been unsatisfactory because of the intricate chemical or serologic technics involved and the wide margin of error (6, 7). Moreover, nothing characteristic has been found in the blood picture of persons suffering from this disease. Sometimes an anemia of the hypochromic type is present which varies in different individuals. According to Rankin and Graham (8),

"So often does this picture of anemia occur that we are of the opinion that no patient should receive a diagnosis of primary or secondary anemia until a thorough examination of the entire colon has precluded the possibility of malignancy in its right half. Also it is axiomatic among clinicians that pernicious anemia should always be differentiated from gastric malignancy (or cancer of the right half of the colon)."

In April, 1945, these authors made the startling statement that almost a year elapses before the average patient with cancer of the colon or rectum has an accurate diagnosis made on him (9). It is indeed easy to confuse a severe type of carcinoma with pernicious anemia, but one is more apt to find a lower hemoglobin count when a neoplasm is present (10).

Variation in the size and shape of the red blood cells has been noted by Gruner and others (11) manifested by poikilocytosis and an unusual degree of polychromatophilia. The finding of nucleated red cells is not common. Changes in the leukocytes are not remarkable except in cases in which ulceration has taken place. In many instances the blood picture remains normal.

Many theories have been proposed to explain the conversion of normal into malignant cells (12). Both the malignant and the non-malignant cell elicit a reaction in the connective tissue. With the non-malignant cell this leads eventually to destruction and removal of the implanted cells, whereas the malignant cell is able to dominate the reaction so as to compel the formation of a stroma which enables the implanted cells to live (13).

The multiplicity of theories regarding the etiology of cancer is reflected in the publications of the American Association for the Advancement of Science which record the present status of cancer research and discuss the virus approach, carcinogenesis, enzymes, diets, and chemotherapy (14). But while we await the solution of the cause of cancer, much may be done to institute proper therapy if early or pre-symptomatic cancer can be discovered lurking in the body.

METHOD

Thus, impelled by the need of finding a simple test for cancer which could be done at the office or at the bedside, and impressed by the simplicity of Goldberger's method of measuring the blood sedimentation rate (15), the author evolved a simple blood test (16). Blood obtained by puncturing the fleshy portion of the patient's finger-tip is allowed to dry in the form of three droplets on a glass slide. In this procedure the finger-tip is held with light but uniformly constant pressure and allowed to touch the under-side of the glass slide lightly three times. The first drop may be too thick or too heavily rimmed or slightly smeared; the second and third drops should form a definite clear pattern if allowed to dry undisturbed on the righted slide in the horizontal position. It is wise to prepare two such slides in case one becomes lost or broken.

The pattern when observed microscopically shows definite characteristics, providing a sensitive indicator of the presence or absence of cancer. The appearance of normal blood is shown in Fig. 2. Note the well defined mosaic appearance or weblike pattern. Much fibrin is present, leukocytes are scarce, and the red blood cells

Submitted Nov. 1, 1951.

are tightly packed with rouleau formation and no variation is seen in the size or shape of the corpuscles.

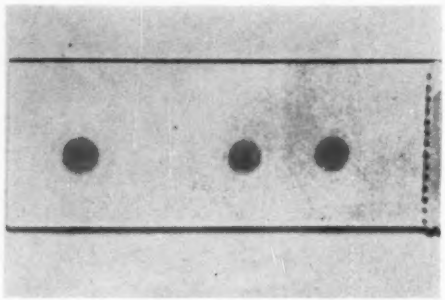

Fig. 1: Macroscopic

After preparing and studying several thousand of these blood slides it became possible to recognize a pattern which appeared to indicate transition or an early breaking down of the normal pattern, as seen in Fig. 3. Fibrin is breaking down in several areas. There are still many red and white cells present in

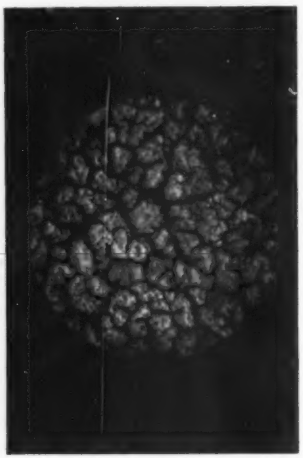

Fig. 2: Negative Pattern

the aggregate and some agglutination with small lacunae and a number of granules. The final stage of full bloom cancer is shown in Fig. 4. Now very few fibrin threads are visible and large amounts of clear interspace or lacunae are seen. Through agglutination, cells are clumped together in masses and the reticular network has entirely disappeared.

These blood patterns have been studied along with clinical and laboratory data and have been found correlative and informative. When cures were obtained by surgery, radium implantation, irradiation, or by a combination of these methods, the pattern changed from positive to negative with a short period of from six to eight weeks. In some instances this blood droplet test pointed to the presence of early carcinoma before there was any clinical or roentgenological evidence. Slides made on ulcer patients some with severe hematemesis, all showed a normal pattern. Likewise, it was negative in other conditions of the gastrointestinal

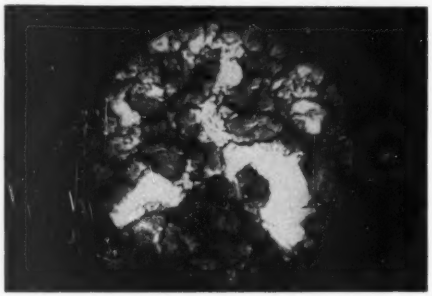

Fig. 3: Early Cancer

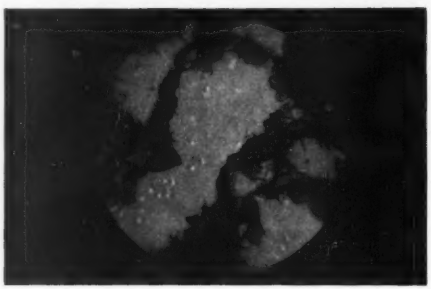

Fig. 4: Full-bloom Cancer

tract, such as regional ileitis, colitis, gastritis, diverticulum, visceroptosis, pylorospasm, and irritable colon.

A few cases are reported in brief to demonstrate the working applicability of this simple test. It is regrettable that it was not always given more credence in the search for the correct diagnosis.

CASE I

E. K., male, age 60, was admitted to a local hospital for dizziness, pains in the knees, weakness of the legs. The diagnosis made at this time was primary anemia, combined sclerosis, and chronic myocardial disease. He left the hospital against advice May 7, 1934, four days after admission.

He was next seen at the office October 6, 1942 complaining of pain in the lower region. He stated that he had been taking liver parenterally and orally since 1934. At this time the blood pattern on the slide was negative. He returned February 12, 1944 with pain throughout the entire abdomen. He consulted a surgeon who did not feel sanguine about operation because of the patient's age and the primary anemia. The blood pattern at this time was positive. The patient consulted another surgeon who made a diagnosis of subacute appendicitis. February 26, laparotomy revealed an atrophic, retrocecal, fibrotic appendix embedded in adhesions. An annular mass in the transverse colon was removed. The pathological diagnosis was adenocarcinoma, undifferentiated and rapidly growing, invading all coats and involving the extraserosal tissue. This patient was discharged April 21. His

bowels moved three times a day through the colostomy and he had one movement via the rectum, but hard stools necessitated straining. He was readmitted July 25 for closure of the colostomy and discharged August 18. He was seen at the office on several occasions and the blood pattern on the slides remained positive. He died July 24, 1945 of carcinoma of the sigmoid colon with metastases to the inguinal lymph nodes.

CASE II

M. B., male, age 59, was first seen at the office December 12, 1945 with the complaint of pain in the lower lumbar region. The blood pattern at this time showed early carcinoma. X-ray films made at the clinic showed only visceroptosis. A general physical examination disclosed no abnormalities. This patient was seen at the office February 15, 1946 and April 9, 1946 and the blood pattern was more distinctly positive. Symptoms persisted. By November 19 the blood pattern was that of full-bloom cancer. At this time stools were loose but contained no gross blood. He refused hospitalization, stating that the lower lumbar pain abated after defecation.

February 20, 1947 he consented to have a gastrointestinal series, and again films were negative. He was now passing three to eight stools a day. In the face of the persistently positive blood pattern a barium enema was done March 1. The radiologist reported no pathology except retention of a large amount of barium from the previous examination.

The following morning the patient was seen at home. He was in shock and was referred to the hospital. He was dehydrated, definitely undernourished. There were expiratory rumbles at the bases of both lungs. The heart was not enlarged. Blood pressure was 100/60. The abdomen was full, hard, almost boardlike, tender on pressure and uniformly spastic. No masses were made out. The impression of the examiner was intestinal obstruction, a perforated viscus in descending colon, stomach, or duodenum.

The patient was prepared for operation. Upon opening the peritoneal cavity free fluid was found with markedly distended loops of small bowel, ascending the transverse colon. Palpation of the rectosigmoid revealed a definite jelly-like mass lying in the hollow of the sacrum; it was movable and involved a segment of sigmoid just proximal to the rectum. Cecostomy was done and transfusions given and continuous oxygen, but the patient died at 11:00 a.m. the following day. Permission was obtained for a post-mortem examination.

The final diagnosis was carcinoma of the rectosigmoid colon with perforation and intestinal obstruction, generalized peritonitis, metastatic carcinoma of the lungs.

CASE III

G. S., a white female, age 24, was admitted to the hospital March 21, 1951 with a history of episodes of acute pain in the upper abdomen, nausea, vomiting and two attacks of hematemesis. A posterior gastroenterostomy was done July 29, 1946 with some relief of symptoms. She had an acute exacerbation of symptoms May 22, 1950 and improved on medical treatment. The diagnosis was "non-functioning gastroenterostomy." She was next seen at the office October 21, 1950, and reported some pain and occasional attacks of vomiting, but no hematemesis or tarry stools. The blood pattern test at this time was positive. A thorough search was made for malignancy at some site but all examinations failed to reveal cancer.

February 25, 1951 another acute exacerbation sent her to the hospital. She was placed on a Sippy régime and discharged improved to return subsequently for further surgery. She returned March 21, 1951. She was thin and pale with a red blood count of 3,600,000 and 10.6 gm. hemoglobin. The blood pattern was positive. A partial gastric resection was still functioning, but it was rather high in the posterior wall and it was thought advisable to resect the pyloric end of the stomach to promote better functioning.

Pathological examination of the pyloric segment of the stomach showed no gross evidence of ulceration of neoplasm. Eight sections were examined microscopically and in one, an area of mucosa 3 to 4 mm. in diameter was seen to contain an early carcinoma *in situ*. The normal glandular pattern of the mucosa had been completely replaced by an atypical proliferation of cells and mitotic figures were frequent. In a few areas the cancer cells were mucin-secreting. Attempts to find any other cancerous tissue in numerous sections cut from the entire specimen were futile. The final diagnosis was carcinoma *in situ* confined to a very small area of the stomach; gastritis involving chiefly the muscularis. Section of a lymph node was negative.

The patient was discharged April 5, 1951. She is to report at frequent intervals for check-up examination. To date the blood pattern has remained negative and she is leading an active life as a nurse with no recurrence of gastric symptoms.

In dealing with these patients, the personal factor must be reckoned with. When a test is made at the office and the pattern of early malignancy appears, it is often difficult to impress upon the patient the gravity of the situation. He is reluctant to go to the hospital for a thorough examination since in many instances he is not ill, or thinks he is not. Then, when he becomes convinced that it is unwise, even dangerous, to procrastinate further, there is the obstacle of the surgeon who may not accept the evidence on the slide. The following cases were taken at random and show the unhappy result of failure to regard the positive blood pattern.

Case IV. M. S., female, 68 years old. Pain in lower quadrant. Constipation. Slight amount of green vomitus on several occasions. Weight loss of 20 pounds in four months. Blood pattern positive. Patient consented to operation six months later. Laparotomy revealed adenocarcinoma of the ascending colon. This patient died at home three and one-half months after discharge from the hospital.

Case V. W. B., male, 64 years old. Began to lose weight, but was able to eat and enjoy food. Felt tired all the time. Examination of the stomach by x-ray was negative. Rigidity of abdominal muscles. Skin somewhat dehydrated. Blood pattern positive. Operation four months later revealed adenocarcinoma of the stomach. This patient died on the fifth postoperative day.

Case VI. A. L., female, age 46. Complained of being anemic and came to office for iron pills. Loss of weight over a period of three months. Patient merely thought she had been working too hard. Slight swelling of abdomen, but no pain nor nausea. Blood pattern positive. Patient would not consent to operation until a year had lapsed. Laparotomy then revealed adenocarcinoma of the stomach with metastases to the kidney. This patient died at home eight months after operation.

Case VII. M. M., female, age 66. Patient stated that she had always been thin and that her stomach had felt upset during the early morning hours. She was able to sleep and eat fairly well. Loss of 22 pounds during the last six months. Positive blood pattern. Patient refused operation until 14 months had passed. Laparotomy revealed adenocarcinoma of the stomach. This patient died at home seven weeks after discharge from the hospital.

Case VIII. W. C., male, age 71. Complaint of vague abdominal discomfort which wakened him during the night. Condition present for five months. On two or three occasions he vomited a small amount of dark fluid. Muscles of abdomen rigid, but no tenderness or pain present on palpation. Blood pattern positive but patient refused operation until six months later. Laparotomy revealed adenocarcinoma of the stomach. He was discharged March 18, 1945 and died 10 months later.

In these and similar cases the blood pattern on the slide was definitely positive, but the patients refused surgery until too late for cure.

DISCUSSION

The early detection of cancer remains a prime requisite in its control and more and more attention is being directed to determining the accuracy of various methods proposed to detect malignancy and to differentiate it from other conditions. The blood pattern test described above has proved itself remarkably correct in the author's experience over a period of ten

years. It is simple, inexpensive, and can be performed in the office during the course of a routine physical examination.

Girón (17), in 1943, reported his results with this test in 515 cases and found that in the cancerous patients the typical positive cancer pattern appeared in 90.4 per cent of the cases. Gruner (18) of Montreal finds it accurate in 98.4 per cent, and runs this test parallel with his own. Coltman (19), Huggins, Miller and Jensen (20), Finnegan and his coworkers (21), Whitney (22), Norman and Slicher (23), Black and Speer (24), Hawk, Inkley and Thoma (25, 26, 27), and Nickel, Berger, and Brickley (28) have reported results of their own tests for cancer or have made extension-studies of cancer tests already in use for more than a decade. Some have run several tests parallelwise in an effort to evaluate efficacy. The accuracy of the results when the author's test is used varies with the clarity of the pattern on the slide and the experience of the examiner.

Körbler and Frank (29) seem to be the first to employ this blood droplet test in animals along with Gruner's test (18) to discover changes taking place in mice subjected to tumor implantation. The very positive reaction in the blood droplet indicated a brief life expectancy in the animals and proved an excellent criterion in choosing mice for experimentation purposes.

CONCLUSIONS

A simple and reliable method of diagnosing normal and cancerous blood by observing a drop allowed to clot and dry on a glass slide is presented. It is suggested that disturbance in the plasma content is the factor which alters the compact pattern of normal blood.

Once the pattern of early cancer is recognized, every effort should be made to locate the malignant lesion and institute prompt therapy.

The test should be repeated at frequent intervals to ascertain results of therapy and to determine the prognosis.

It is hoped that the routine use of this simple method will furnish a clue to the presence of cancer, make possible earlier diagnosis, adequate therapeusis, and achieve a greater percentage of cures.

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THE RELATIONSHIP BETWEEN COLITIS AND PYORRHEA ALVEOLARIS

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ETIOLOGY AND TREATMENT OF PYORRHEA ALVEOLARIS

Pyorrhea alveolaris is defined as a progressive inflammatory and degenerative change in the periodontium which is characterized by purulent discharge from the alveoli of the teeth. The condition is also known as periodontoclasia, periodontosis, suppurative pericementitis, Rigg's or Fauchard's disease.

The etiology is either local or systemic. Among the local causes Goldman (1) gives the following causes: irritation of any kind, neglect of oral hygiene, loss of contact between the teeth resulting in marginal periodonitis; food packing against the gingiva resulting in inflammation and bone resorption. The causes of loss of contact may be caries of the proximal occlusal type, faulty fillings, overhanging fillings, ill-fitting crowns, faultily designed clasps, calculus, materia alba, and mucus plaques. Functional insufficiency due to lack of exercise in mastication, and in certain teeth having no antagonists or open bite, results in disturbances in the supporting structures and increased susceptibility to infection and lowered local resistance Among the other causes are occlusal trauma, loss of teeth or nonreplacement of missing teeth, crowding of teeth, unilateral mastication, bruxism, faulty use of toothpicks and faulty toothbrushing. Merritt (2) believes that bacteria in the oral cavity are essential to start periodontal inflammation. Moreover, Martzell (3) claims that streptococcus and staphylococcus are the chief factors in the causation of pyorrhea. Thoma (4) states that *S. aureus, S. albus,* streptococci, pneumococci, streptobacilli, spirilli, treponema, streptothrix and various types of fungi have been isolated from pyorrhea. Ivy, Morgan and Farrell (5) fed normal dogs the soft diet which was intended for gastrectomized animals. These animals showed early evidence of periodontal diseases and tendency toward calculus formation. King and Glover (6) fed bread and milk or raw meat and milk to ferrets. Within 8 to 12 weeks, there was gingivitis, calculus formation, atrophic changes, and loosening of teeth. The addition of short lengths of bone to the diet caused recovery of most of the symptoms. Craig and Faust (7) state that the incidence of *Endameba gingivalis* is high in individuals with pyorrhea alveolaris and other suppurative conditions of the teeth. This parasite is also found in 10 per cent of well-cared for and healthy mouths. They also quote Hinshaw and Kofoid, Hinshaw and Johnson that *E. gingivalis* can produce infection in dogs showing inflammation of gingival tissues. However, the parasites disappear spontaneously and there is no increase in the severity of the lesions. Similarly, *Trichomonas tenax* is found in the human mouth in the tartar around the teeth, in the cavities of carious teeth and in pus pockets in cases of pyorrhea alveolaris.

Miller and Firestone (8) believe in psychosomatic dentistry, and that there is a relationship between mental well-being and the health and integrity of the oral tissues, emotional tension creating oral disease through disturbances of functions.

Disturbances of the general health and nutrition of the body frequently produce marked changes in the vital resistance of the gingival and periodontal tissues and render them more susceptible to injury from traumatic stresses and bacterial invasion (1). The circulation of the gingival tissues is subject to changes in the general body health. Systemic factors probably reduce the resistance of the tissue and thus make it more vulnerable to local factors and give rise to periodontal disease. Glickman (9) found that when the normal tendency toward bone formation was inhibited because of systemic disease, the barrier against bone destruction stimulated by inflammation was diminished and the resultant bone loss was severe. Systemic infections (1) which may have oral manifestations are endocrine dysfunctions such as hyperparathyroidism, hyperthyroidism, hypofunction of the anterior pituitary, hypofunction of the gonads (10, 11) etc; allergy, blood dyscrasias such as leukemia, pregnancy, Hodgkin's diabetes, chronic low grade infections or fevers which undermine the vitality and resistance of the body (1, 12); autoinfection or autointoxication, hypertension, scleroderma (1); increase in the alkalinity of tissue fluids and acid base and calcium phosphorous balance (15): rarefaction of the bone due to disturbances of calcium metabolism (16); and disturbances of uric acid metabolism (17).

Pretel and Robert (18) state that pyorrhea is present in 50 per cent of chronic intestinal conditions. They believe that it is a very frequent symptom of chronic intestinal infections. *Escherichia coli* and Enterococci are absorbed or penetrate the intestinal wall, and become localized in various parts of the body including the gums, giving rise to gingivitis and pyorrhea. This theory is supported by the fact that autogenous vaccines prepared from these bacteria give favorable results.

Studies which are presented in this paper were first observed in a patient who was suffering from amebiasis and pyorrhea alveolaris. During the course of antiamebic treatment, it was observed that there was a steady improvement of pyorrhea with the disappearance of pus pockets, necrotic tissues and inflammatory reaction. It was felt that there was a close correlation between the intestinal pathology and the oral pathology. A thorough study of pyorrhea alveolaris was undertaken from the dental, medical and laboratory aspects.

Following the dental diagnosis of pyorrhea alveolaris, the patients were referred for a thorough medical work-up which included a detailed clinical history particularly of the gastrointestinal tract, thorough physical examination and a complete laboratory work-up.

Smears were made from the pus of the pyorrheal pockets, and stained with Gram and Wright stains. Pus was also cultured in Avery's broth, blood agar

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plates and anerobic cultures. In the beginning total bacterial counts of the oral bacteria were performed by using a modified technic of Henderson and Seneca (19) but this was discontinued since no additional information was obtained.

The stools were examined for parasites especially *Endameba histolytica* by direct examination and cultural methods. Stool cultures for Shigella, Salmonella and streptococci were also done routinely.

Intestinal bacteria counts were routinely performed in all cases. The stools were collected in sterile Petri dishes and the total as well as coliform organs were estimated using the Henderson Seneca method (19).

Complete blood counts including red and white cell counts, hemoglobin estimation and sedimentation rates were also done. Cephalin flocculation and icteric index determinations were performed in patients suspected of hepatic insufficiency. Biochemical determinations were not revealing, therefore they were discontinued.

Case 1. D. D., 43-year-old business executive, had abdominal pains, pain in the right upper quadrant, heaviness, distension and epigastric pain following meals which began gradually in 1946. He lost weight, strength and appetite. Routine physical examination was unrevealing. He was admitted to a hospital where gallstones were discovered, by x-ray. Following cholecystectomy in 1948, the patient felt a little better, but in a short time his symptoms came back with a greater fury, his weight going down from a normal of 175 lbs. to 125 lbs. He could not even eat bland diet because the abdominal pains increased in intensity. A gastrointestinal series was negative. He was readmitted to the same hospital and was told that he had pancreatitis for which a second operation was planned. Disappointed in his condition, patient left the hospital against advice. He was advised by J. K. to have a consultation in relation to his gastro-intestinal condition. It should be mentioned that this patient was under the care of J. K. for a pyorrheic condition of his teeth for several years, which did not respond to dental treatment.

A routine clinical history in this patient revealed that he had occasional attacks of diarrhea and constipation, but there was no history of dysentery. However, since he had had extensive travels in Europe and Middle East, amebiasis was suspected. Physical examination revealed an asthenic individual who had lost a lot of weight; the teeth showed extensive pyorrhea, the heart and lungs were normal, liver was two fingers palpable and tender, the sigmoid and caecum were tender and thickened, the reflexes were exaggerated. Stool examination revealed trophozoites of *Endameba histolytica*, culture was negative for Salmonella Shigella, total bacterial count of the stools was 32,480 billion bacteria per gram of wet feces, 14,560 billion being coliform organisms. Hemoglobin 76%, E. S. R. 5mm/hr., W. B. C. 8,800 and R. B. C. 4.26 million. The urine was negative for albumin, glucose and urobilinogen, while the icteric index was 5 units, and cephalin flocculation was plus-minus.

The treatment was immediately started with 0.75 gram chiniofon (three tablets) three times daily after meals for ten days, followed by Thalamyd, 1.5 gram (three tablets) three times daily after meals for the second ten days. Iron, vitamins, liver extract and methionine were also prescribed to build up the hemopoietic system and the liver. Within ten days the pains disappeared, the appetite came back and the patient began to put on weight and strength. A month after the medication, a dental consultation revealed that the pyorrhea had subsided and in the course of time the condition was markedly improved and almost cured. This patient had repeated stool examinations for ameba and stool counts. The ameba disappeared completely, and the stool flora was within normal limits. Treatment was continued for a period of five to six months.

This case gave us the idea that there could be a relation between colitis and pyorrhea; however, it was not clear whether it was amebiasis,secondary bacterial colitis or the general malnutrition or intoxication and lowered resistance.

Case 2. A. T. This 22-year-old female secretary had bleeding gums for five years. The past and present clinical history were negative except for constipation and occasional attacks of diarrhea; physical examination was essentially negative. Stool culture was negative for Shigella-Salmonella, but positive for *Streptococcus fecalis*, while parasitological examination was negative. Total fecal bacterial count was 18,000 billion per gram wet feces, coliform organisms 15,600 billion, E. S. R. 18mm/hr and the blood revealed a mild secondary anemia.

One and one-half grams Thalamyd was administered three times daily after meals for ten days, a rest of ten days was given and then a second ten-day treatment with Thalamyd. This treatment was continued for about three to four months. Her gastro-intestinal symptoms were corrected, colitis was cured and pyorrhea improved.

Case 5. V. H. 47-year-old businessman had pains and aches in joints and muscles and pyorrhea for twenty years. There were no gastro-intestinal complaints, and the past history was not instructive. However, his strength was beginning to fail and he was getting fatigued easily. Physical examination revealed arcus senilis, a tender, and two and one-half fingers enlarged, liver. A clinical diagnosis of hepatitis was made. Stool examination was negative for ameba, Salmonella-Shigella, but positive for *Streptococcus fecalis*. Intestinal bacterial count was somewhat elevated, E. S. R. was 18mm/hr., there was mild secondary anemia, the urine was normal urobilinogen negative, icteric index 4, and cephalin flocculation negative. Thalamyd, vitamin, iron, methionine, phenobarbital were administered. Patient not only got symptomatic relief, but also his pyorrhea was improved.

Case 8. A. O. 29-year-old housewife was a victim of pyorrhea for several years. For many years, she was having vague gastro-intestinal symptoms, abdominal pains and cramps, constipation, underweight, lack of pep, appetite and strength. Her B. M. R. was low; therefore, she was given thyroid. She had a hemorrhoidectomy. Emotionally she was very disturbed, because being married nine years she never became pregnant. She was told that she had an infantile uterus and that without an operation, pregnancy was out of the question. She wanted a child, but dreaded the idea of the operation. The physical examination was essentially negative except for underweight and an enlarged tender liver. A previous barium enema revealed spastic colon. Stool examination revealed cysts of *E. histolytica*. The total intestinal bacteria count was 13,440 billion/gram feces and 700 billion coliform organisms/gram feces. The blood showed a microcytic hypochromic anemia and E. S. R. was 14 mm/hr. She was given 0.75 grams chiniofon three times daily after meals for ten days, followed by 1.5 grams Thalamyd three times daily after meals for another ten days. These drugs were used alternately for about four months. Iron, vitamins and thyroid extract were also given. Stool examinations during and after the treatment were negative for ameba. Within a short time the gastro-intestinal symptoms and constipation disappeared, and the patient became pregnant. She is now in her fifth month and is going through a normal pregnancy. Pyorrhea is markedly improved. This case shows the importance of the colon as a focus of infection or intoxication acting on the general health, gums, liver and the reproductive system.

Case 18. L. B. 43-year-old housewife had pyorrhea and constipation for ten years. The constipation was so severe that the bowels moved once every five days and only after an enema or suppository. Oral laxatives had no effect. She was highly irritable and nervous and this led to attacks of frequent urination. Appetite was good but she had epigastric discomfort and eructations. The patient got tired easily and had sensation of numbness in her muscles. There was no history of dysentery, but she had had puerperal sepsis 18 years ago. She was going through early menopause. Physical examination revealed pyorrhea, geographical tongue and a liver enlarged two fingers and tenderness in right lower quadrant. Stool examination was negative for Shigella-Salmonella,

ameba and streptococci. The total fecal bacterial count was 3,600 billion/gm. feces and coliform organisms 1800 billion/gm. feces. Sedimentation rate was 26 mm/hr. She had microcytic, hypochromic anemia but there were no pathological findings in the urine. In view of the elevated intestinal bacterial count, the patient was put on Thalamyd, 1.5 grams three times daily after meals for ten days, a rest period of a week and a second ten-day Thalamyd treatment. This treatment was supplemented with buccal pellets of estradiol, and liver extract injections. The bowels became normal, and the gastric symptoms disappeared, while the pyorrhea improved. She has been under treatment for 3 months. This case illustrates that even though there were no pathogenic organisms, yet the increased intestinal bacteria was responsible for constipation and colitis. Colitis was corrected through the use of Thalamyd; the bowel movements became normal, and the rest of the gastrointestinal tract began functioning normally. Again the correlation between the tissues of the mouth and that of the colon.

CLINICAL FINDINGS IN PATIENTS OF PYORRHEA ALVEOLARIS

TABLE I

No.	Name	Pyorrhea alveolaria Severity	Duration	GI findings	Complications	Treatment	Results
1.	D.D.	Severe	10 years	Diarrhea; Constipation; Pain, Cramps; Loss weight	Cholecystectomy; Hepatitis; Amebiasis	Chiniofon; Thalamyd; Iron-vitamin; Liver extract; Methionine	Amebiasis and hepatitis—cured; Pyorrhea—markedly improved
2.	A.T.	Severe	5 years	Diarrhea; Constipation	Colitis (strep)	Thalamyd; Iron; Vitamins	GI symptoms—corrected and colitis—cured; Pyorrhea— improved
3.	V.B.	Severe		No complaints		Thalamyd; Iron; Vitamins	Pyorrhea—improved
4.	G.E.	Very Severe	7 years	Pain; Indigestion	Peptic ulcer; Hemorrhage; Spastic colon	Ulcer treatment; Thalamyd	Ulcer and pyorrhea improved
5.	V.H.	Severe	20 years	Joint and Muscle pains	Colitis (strep); Hepatitis?	Thalamyd; Phenobarb; Methionine	Colitis and hepatitis—cured; Pyorrhea—improved
6.	A.C.	Moderately Severe		No complaints		No follow up notes	
7.	P.P.	Very Severe		Diarrhea; Dysentery? Chest Pains	Liver dysfunction?	Thalamyd; Phenobarb; Methionine Belladonna	Relieved of symptoms; Pyorrhea—markedly improved
8.	A.O.	Severe		Constipation; Hemorrhoids; Cramps	Amebiasis; Sterility	Chiniofon; Thalamyd; Vitamins; Iron; Thyroid ext.	Pyorrhea—markedly improved; Pregnant now; Amebiasis—cured
9.	N.H.	Moderately Severe		Indigestion; Pain, Cramps	Duodenal ulcer hemorrhage	Treatment not followed	
10.	W.P.	Very Severe	1.5 years	Dyscatery; Malnutrition	Amebiasis; Hepatitis	Chiniofon; Thalamyd; Iron; Vitamins	All cured; Pyorrhea—cured
11.	H.A.	Severe	1 year	Diarrhea and Constipation		Thalamyd; Vitamins; Iron	Improved
12.	E.K.	Severe	11 years	Indigestion	Colitis (strep)	Thylamyd; Iron; Vitamins	Improved
13.	W.W.	Severe	3 years	Constipation; Diarrhea	Colitis (strep)	Thalamyd	No follow-up notes
14.	A.A.	Severe	20 years	Nervous stomach	Colitis (strep)	Thalamyd; Vitamins	No follow-up notes
15.	A.C.		3 years	Diarrhea; Underweight; Pruritis; Abdominal cramps	Colitis (strep)	Vitamins; Thalamyd; Iron; High caloric diet	Colitis—markedly improved; Pyorrhea—markedly improved
16.	H.T.		2 years	Diarrhea; Constipation; Mucus in stools; Cramps, pains	Colitis; Hepatitis	Thalamyd; Vitamins	No follow-up notes
17.	N.F.		8 years	Nervous stomach	Colitis (strep)	Thalamyd; Iron; Vitamins	Colitis under control; Pyorrhea—improved
18.	L.B.		10 years	Chronic constipation; Flatus Irritability; Headache	Colitis	Thalamyd; Vitamins; Iron; Liver Ext.; Estradiol	Colitis under control; Pyorrhea—improved
19.	H.G.		10 years	Constipation		Thalamyd	Improved
20.	A.K.		5 years	Underweight Diarrhea	Malnutrition; Colitis	Thalamyd; Iron; Vitamins; Liver Ext.; High caloric diet	Malnutrition corrected; Colitis and Pyorrhea—improved

RESULTS

Table I shows in a tabular form the main clinical features in twenty cases of clinical pyorrhea alveolaris. The duration of the disease ranges from one to twenty years while most of the cases are severe or moderately severe manifestations of oral infection. When a detailed medical history was taken on these patients, almost all had some kind of gastro-intestinal complaints even though such complaints were not significant in the opinion of the patients, because they were not severe enough to disturb the patient materially. The oral complaints were far more important than the gastro-intestinal complaints. The authors believe that the oral complaints should be considered as part of the gastro-intestinal system even though the patients do not realize that the mouth including the teeth is a part of the alimentary canal.

dysfunction or hepatitis was suspected. Two patients had duodenal ulcers.

All patients had *Treponema vincenti* and *Bacillus fusiformis* in the pus obtained from the pockets of pyorrhea. Four had a mild microcytic, hypochromic anemia. The sedimentation rate was increased in 13 cases.

The stool cultures were negative for Salmonella and Shigella group. The total bacterial count as well as the coliform bacteria were increased in all the cases. Whereas the normal count is 140 billion/gram wet feces for the total bacteria, and 122.5 billion/gram for the coliform organism (19), the mean total bacteria count in pyorrhea alveolaris is 8,643.6 billion/gram and the coliform organism is 4,513.6 billion/gram. This means that the total bacteria is increased 37-fold in comparison with the normal.

The treatment administered to these patients was mainly medical. The dental treatment included frequent dental consultation for checking on the progress of the condition.

TABLE II

LABORATORY FINDINGS IN PYORRHEA PATIENTS

No.	Name	Intestinal Bacte (bil./Gm wet fe Total	Coliform	Pathogen	E.S.R.	Hb.	W.B.C.	R.B.C.	Gum Smear
1.	D. D.	32,480	14,560	E. histolytica	5mm/hr	76%	8,800	4.26 mil.	T. vincenti B. fusiformis
2.	A. T.	18,000	15,600	S. fecalis	18	86	5,400	4.37	T. vincenti
3.	V. B.	3,040	2,040		19	78	7,800	4.1	same
4.	G. E.	700	90		9	90	12,050	5.65	same
5.	V. H.	690	280	S. fecalis	18	79	8,600	4.35	same
6.	A. C.	13,600	11,200		20	78	12,200	4.09	same
7.	P. P.	610	510		8	79	9,000	4.7	same
8.	A. C.	13,440	700	E. histolytica	17	85	8,900	4.18	same
9.	N. H.	12,640	10,080	G. lamblia	12	94	6,850	5.37	same
10.	W. P.	2,520	2,240	E. histolytica	16	83	6,350	4.03	same
11.	H. A.	2,800	2,540		15	79	8,950	4.05	same
12.	E. K.			S. fecalis	13	80	6,550	4.3	same
13.	W. W.			S. fecalis					same
14.	A. A.	2,120	960	S. fecalis	10	87	9,950	5.1	same
15.	A. C.	2,200	1,040	S. fecalis	12	80	13,300	3.99	same
16.	H. T.	3,760	3,080		8	86	10,150	5.05	same
17.	N. F.	36,000	11,200	S. fecalis	25	68	8,100	4.14	same
18.	L. B.	3,600	1,800		26	74	8,500	3.81	same
19.	H. G.	2,100	1,100		2	83	8,500	4.76	same
20.	A. K.	5,280	2,220		6	81	6,400	4.00	same
Average Bacterial Count		8,643.6	4,513.6						
Comparison with normal		61.7-fold	37-fold						

With the exceptions of Cases 3 and 6, all complained of gastro-intestinal symptoms. The commonest symptom was constipation, or occasional diarrhea followed by constipation, vague abdominal pains and even cramps, sour eructations, belching, gastric distension, anorexia, heaviness after meals, loss of weight, lack of pep vigor and vitality easy fatigability sometimes muscle and joint pains and headaches and dizziness. Fourteen of 20 patients were clinically suspected of colitis, three proved to be amebic colitis, and seven streptococcic colitis. In the remaining four cases no etiologic factor could be found. In five patients hepatic

The medical treatment was both specific and general. In those cases where the diagnosis of amebic colitis was made, the patients were administered chiniofon, three tablets three times daily for ten days followed by three tablets of Thalamyd three times daily for another ten day. This treatment was continued for two to four months. The secondary anemia and hepatic dysfunction were treated with iron, vitamins, liver extract and methionine.

In streptococcic colitis, the treatment included the

routine use of Thalamyd, three tablets three times daily for ten days, followed by a rest of a week and another ten days treatment. This routine was carried out for 2 to 4 months. The secondary anemia was treated with iron, vitamins and liver extract.

At the time of the writing of this paper, one patient is definitely cured of pyorrhea alveolaris, five patients are markedly improved, twelve are improved, and two patients still have to be checked. As the colitis improved, and the bowels became normal, the improvement in the condition of the gums became apparent. In some of the patients the improvement in the gums was apparent within two weeks of treatment, while in most of the cases, the improvement began in about two months. With the regulation of the intestinal function, the pus pockets in the gums collapse, the inflammatory reactions subside, the edges of the gum become more adherent to the teeth and the general trophic condition of the gum approaches that of the normal gum. It should not be forgotten that in all the patients with pyorrhea there is a certain degree of halitosis. This unpleasant breath odor disappears with the healing of the inflamed gum. The patients who were underweight began to put on weight, the appetite improved and the anemia was corrected.

In those cases where no specific organism was detected in the stools, the treatment with Thalamyd was administered for the sole purpose of reducing the intestinal bacterial count to the normal. Again in these cases we had to use the intermittent administration of a sulfa drug, because the continued use gives rise to resistant mutant forms and that there is the probability that vitamin synthesizing bacteria will be completely inhibited giving rise to avitaminosis.

When Thalamyd is administered, whether conjointly in amebic colitic or in streptococcic colitis or in colitis in which there is no specific organism except an overall increase of the intestinal bacterial flora, the bacterial count is reduced to normal during the course of the treatment.

Local treatment consists of the removal of calculus, cleaning of the pus pockets, removal of necrotic tissue and application of packs of phthalylsulfacetimide to the inflamed gums and pockets.

DISCUSSION

The oral cavity and its contents are derived from the ectoderm, and are lined with stratified squamous epithelium while the colon is derived from the endoderm and is lined with columnar epithelium. Despite this difference in the origins of these two segments of the gastrointestinal tract, it seems that from the point of view of pathology, there is a definite correlation between the colon and the gums or gingival membrane. Eighteen of 20 patients (90%) complained of gastrointestinal disturbances. Three of these cases were confirmed cases of amebiasis, another seven had streptococcic colitis. Four cases of clinical colitis where no specific organism was isolated from the stools showed an increase in the fecal bacterial count.

In ulcerative colitis the total intestinal bacteria are increased 85-fold while the coliform organisms are increased 50-fold (20). It is theorized that the ulcerations in the colon in chronic ulcerative colitis are the result of excessive production of lysozyme (21). It is very likely that the increase in the lysozyme titer in chronic ulcerative colitis is due to the increase of the normal intestinal bacteria (20) which also produce other proteolytic enzymes.

In pyorrhea alveolaris patients with or without colitis, with or without the presence of a specific pathogenic organism in the intestinal tract, the normal intestinal flora is increased 61.7-fold while the coliform organisms 37-fold. This increase in the bacterial flora in the colon is probably associated with an increase in amount of enzymes produced (lysozyme, proteolytic enzymes) which in turn could be absorbed into the system and exert the lytic action on the gingivae. Once there is an erosion of the gingivae, the bacteria in the mouth invade the lesions and start the inflammatory reaction.

A second factor of importance in diseases of the colon is the disturbance of absorption and assimilation of the essential food elements. Thus the body being deprived of these, there will be a lowering of the general resistance as well as the local resistance in the mouth.

A third factor is the stagnation of the stools due to constipation resulting from the atony of the intestinal musculature. With stagnation, there is putrefaction and autointoxication, acting as a major focus of infection, thus impairing the vitality and tonus of the body in general.

Regardless of what theoretical explanation we can find concerning the relationship between the oral cavity and the septic colon, one thing remains clear. As soon as the specific pathogen is destroyed, or the colon begins to function as a normal organ and the total number of intestinal bacteria are brought down to the normal level, the pyorrheic lesions begin to show signs of improvement and with further medication, all the lesions will disappear and the trophic condition of the gums becomes normal.

The normal intestinal bacteria apparently assume a certain degree of invasive or pathogenic properties especially when there is colitis. With the use of sulfonamides or antibiotics, these organisms are completely destroyed, and the intestine acquires new flora which probably does not have the virulence the predecessor had. This gives time for the colitis to subside, and the production of the toxic bacterial metabolites is reduced, thereby limiting the activity of the colon as a focus of infection.

It is our experience that local treatment of pyorrhea by the dental technic should be boiled down to cleaning of the pockets, and the denuding of the necrotic tissues, removal of calculus and application of Thalamyd paste. It is a medical and dental problem and it should be handled conjointly by the dentist and the gastro-enterologist.

Etiological causes and therapeutic results indicate that there are two types of pyorrhea alveolaris. The simple or the local type is the result of some local factor or factors. This is purely a dental problem, a self-limited disease, which does not spread from one tooth to the other, and the treatment is quite simple. The generalized or the systemic type of pyorrhea alveolaris usually involves quite a number of teeth, and as the disease is neglected, it spreads to the adjacent teeth

so that in time all the teeth are involved. Local factors are not important in this class of pyorrhea. The cause of this condition should be thoroughly investigated by a competent gastro-enterologist and a thorough search for some distant infection, active or latent, in the colon should be kept in mind. Frequently, the other systemic symptoms dominate the symptoms of colitis. We recommend the following procedure in the management of pyorrhea alveolaris:

1. A detailed clinical history, especially of the gastro-intestinal tract for such symptoms as constipation, diarrhea, flatulence, vague abdominal pains or cramps, distension after meals, sour eructation, and disturbances in digesting the food. The patients should be questioned concerning the history of shigellosis, amebiasis, and colitis.

2. Thorough physical examination, which should include the condition of the stomach, colon, and the liver.

3. Thorough dental consultation, including x-ray studies of the teeth and detection of other abnormalities of the teeth or mouth.

4. Complete blood studies, including the red and white cells, E. S. R., urinalysis, liver function tests, and stool examination for *E. histolytica,* culture for pathogenic bacteria and bacterial counts.

5. The treatment should be directed against the specific pathogen. The total bacterial count should be brought to normal limits through the use of soluble but non-absorbable sulfonamide. The treatment should be continued until the gastro-intestinal symptoms disappear, colitis is cured and pyorrheic condition of the teeth disappears. The treatment may have to be carried on for several months. Meanwhile the secondary anemia should be corrected through the use of iron, vitamins, and liver extract. If there is any indication that the hepatic function is impaired, the patient should be put on high carbohydrate, high vitamin and high protein diet, avoiding fats, and methionine and choline should be administered. During the course of the treatment, stool counts should be made to determine the number of intestinal bacteria.

SUMMARY AND CONCLUSION

1. Eighteen or 90 per cent of twenty cases of pyorrhea alveolaris manifested symptoms of gastrointestinal system. In fourteen or 70 per cent of the cases, the clinical diagnosis of colitis was made. Three of these cases were caused by *Endamoeba histolytica,* and seven by *Streptococcus fecalis.* The remaining four patients did not have any pathogenic organism.

2. In pyorrhea alveolaris, the total number of normal intestinal bacteria is increased 61.7-fold, while the coliform organisms are increased 37-fold.

3. When the specific pathogenic organism causing colitis is destroyed, or the normal intestinal bacteria are reduced to normal levels in specific or non-specific colitis, pyorrhea is immediately brought under control, and in due time marked improvement in the condition of the gingivae is noticed, and some cases are even cured provided the treatment is adequate.

4. The best method of curing colitis and in turn the resulting pyorrhea is to give the specific treatment, and the use of a non-absorbable but soluble solfonamide such as Thalamyd. The secondary anemia and hepatic dysfunction should also be given the necessary treatment.

5. It is obvious from the etiological and therapeutic data available that pyorrhea alveolaris is either a local disease, the result of local disturbances in the mouth, or a systemic disease, the result of disease or disturbance of the lower intestinal tract, i.e., the colon. Whereas the former is strictly a concern of the dentist, the systemic or generalized type of pyorrhea should be handled by the dentist and gastro-enterologist.

6. Local pyorrhea does not lead to systemic or generalized pyorrhea. It is our opinion that pyorrhea is not a contagious disease.

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THE ROENTGENOLOGICAL APPEARANCE OF THE GASTRIC MUCOSA IN BLOOD DISEASES*

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THE HISTOLOGICAL changes of the gastric mucosa in blood diseases, and principally in pernicious anemias, are well known after Fenwick's, Faber's and Bloch's works.

However, Castle's famous experiments concerning the importance of the gastric secretion in the development of the red blood cells were actually the origin of numerous researches of this field.

At the present, everybody knows the importance of the mutual relations between the blood diseases and the pathological changes of the gastric mucosa.

The principal changes are the following ones: gastric cancer, polyposis and gastritis.

The efficiency of the roentgen investigation in discovering carcinoma and gastric polyps, even if very small, is, in our opinion as good, if not better, than clinical or gastroscopic examination.

In the study of gastritis, however, gastroscopy proves more efficient than X-ray examination.

This relative inferiority of radiology, resulting from technical and interpretational difficulties, induces us to consider here only gastritis.

To the same extent as benign or malignant tumors, gastritis in relation with blood diseases has, radiologically speaking, nothing specific. They belong to the general group of gastritis with their principal variants.

The changes of gastric mucosa can reveal either atrophy or proliferation.

In red cells diseases, the hypertrophic status is provocated by edema, inflammatory infiltration, hypertrophy of glands, hypertrophy of the muscular fibers or several of these factors.

In white cell diseases, the gastric mucosa can take a hypertrophic aspect as a consequence of a mass infiltration of ripe white cells, young or metaplastic forms.

Whatever the change of the gastric mucosa in blood diseases may be, atrophy or hypertrophy, the alterations of the stomach folds can become macroscopic and must, therefore, appear in radiologically detectable signs (Berg, Gutzeit.)

A rather true radiographic visualization of the gastric internal pattern can generally be obtained by utilizing a proper technique. This technique consists of the following points: spreading of a small quantity of barium in a "thin layer," palpation under screen and change of positions. But the difficulty only starts when interpreting the pictures as it is not always possible to notice whether the alterations observed are on account of gastritis or merely on account of a functional phenomenon.

Indeed, Forssell's remarkable works, demonstrating how the mucous relief can be altered by the autonomous movements of the mucosa, induce the radiologist to be extremely careful when interpreting the images of the gastric folds.

Alterations of the gastric mucosa leading to atrophy happen very often in cases of either hypo- or hyperchromic anemias. Practically all gastroscopists agree upon this point. They even can be found in polycythemia. (Desneux).

Radiologically, the symptoms of atrophy of the mucosa appear in narrow, smooth and close-set folds. The tonus and motoricity are either diminished or not. Secretion troubles, if any, do generally not appear radiologically.

Hereunder is a personal case: the clinical symptoms and gastroscopic as well as radiological aspects are typical (fig. 1.).

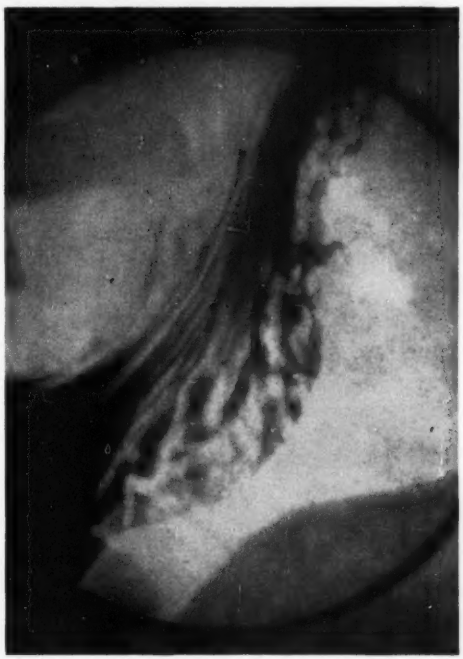

Fig. 1: Atrophic gastritis in a male of 35 years suffering from Biermer's anemia. Gastroscopic diagnosis was: "atrophic gastritis in areas." Compression views.

The patient is a man of 35 years suffering from Biermer's anemia, advancing by stages. The diagnosis based upon hematological examinations and myelograms is not questionable. The gastroscopy reveals several areas of atrophic gastritis. The X-ray examination made be-

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tween two anemia stages does not show any fluid stasis in the stomach, the barium gets spread very easily in a "thin layer" and adheres properly to the walls, allowing us to exclude the presence of mucus. The gastric tonus and motoricity are normal. The folds of the body of the stomach, and particularly those of the "Magenstrasse" are extremely thin, smooth and very close-set. They are deformable and change direction by compression.

Before closing this chapter it should, however, be noted that in some cases of atrophic gastritis, associated with anemia, the gastric folds keep a normal radiological aspect; this is apparently due to the capacity of muscularis mucosae to produce folds even with an atrophied mucosa (Buckstein, Lubarsch, Teschendorf.) On the other hand, if pictures of smooth and narrow folds usually correspond to atrophy of the mucosa, they can as well result from a diminution of tonus and turgor of the submucosa (Buckstein).

Contrary to the atrophic variety, hypertrophic gastritis in anemia happens very seldom: "They more likely correspond to a peculiar deviation of the degenerative process." (Dumont-Ruyters.)

They have been noticed on relapses of pernicious anemias by Jones, Benedict and Hampton. Eibach mentions a polypoid gastritis in a case of progressive secondary anemia. We have had the opportunity to observe three cases of giant gastritis in relation with anemias.

As a consequence of the important changes they bring about in internal gastric relief, they can rather easily be detected by X-ray examination. However, as to the interpretation of the images, the reservations made on atrophic gastritis should be maintained in these cases.

In fact, a hypertrophic gastritis diagnosed by endoscopy can reveal normal radiological aspects (Bockus, Prévôt) and, inversely, images of enlarged and twisted folds could simply result from functional or allergic troubles, any inflammatory or infiltrating phenomenon of the mucosa excepted (Berg, Bockus, Forssell, Prévôt, Templeton, Velde).

Bearing in mind this reservation, hypertrophic gastritis can, at the present, be radiologically diagnosed, with rather great precision. Berg and his collaborators Prévôt and Bücker have particularly studied the changes of the gastric mucosa and have gathered radiological criteria.

Hypertrophic giant gastritis (or plastic pangastritis, according to Bücker) have the following radiological characteristics, observed in our personal cases:

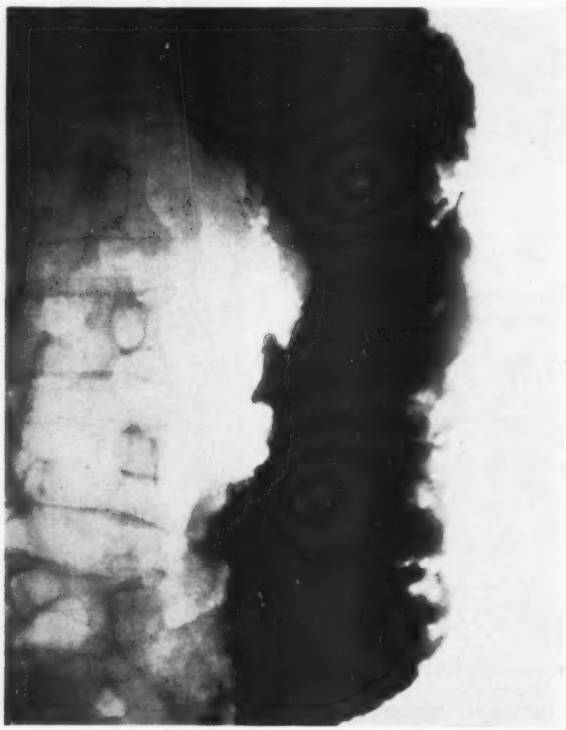

Fig. 2: Giant hypertrophic gastritis in a case of hypochromic anemia. See details in the text. Filled stomach in horizontal position.

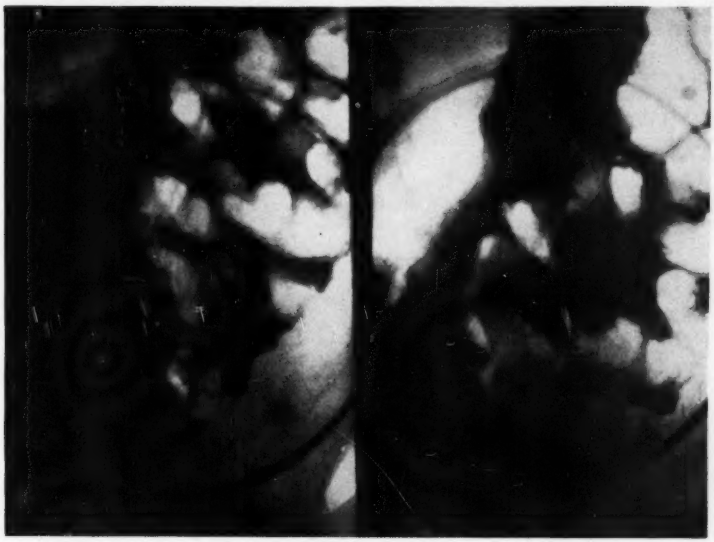

Fig. 3: Same case as fig. 2. Compression views in vertical position taken during the same examination.

—Gastric folds are enlarged and have a disordered construction.

—They are hard and tense.

—Gastric walls are stiff.

—Lesser curvature shows indentations of different sizes and shapes.

It can also have following symptoms:

—Secretion fluid and mucus are abundant.

—The barium, when mixing with the gastric juice, rich in mucus, leads to the "mucous phenomenon" described under the name of "Schummerung" by Berg.

—The walls, especially those of the antral area, are inclined to spasmodic contractures called "Krampftumoren" by Schwartz, because of their resemblance to neoplastic infiltrations.

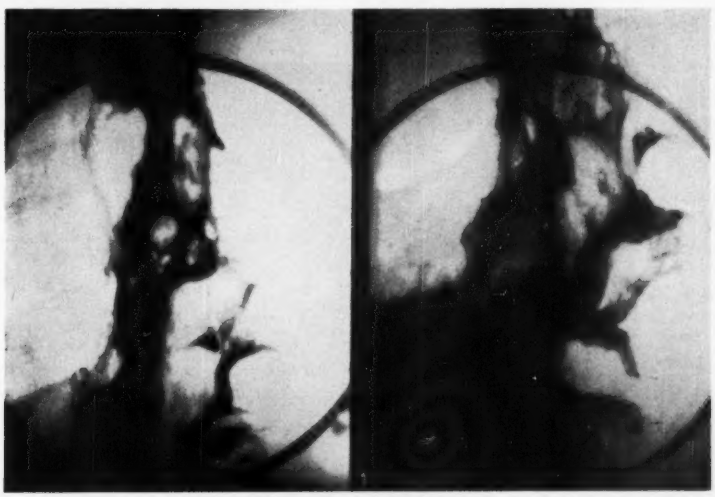

Fig. 4: Same case as fig. 2 and 3, fifteen months later. Compression views in vertical position.

We are giving below a few short observations of our first case of that group:

The patient is a man of 47 years, affected by chronic bronchitis. After meals, he suffers from irregular epigastric pain, meteorism and eructations. He also loses appetite and considerable weight within a short time.

The hematological examination reveals a moderate anemia of hypochromic type (red cells: 3,800,000, Hemoglobin 70%, color index: 0.92.)

The gastric tube sucked up a hypochlorous juice. Bordet-Wasserman's as well as Meinicke's reactions were negative.

The X-ray examination shows an enlarged stomach having from the upper pole to the pre-antral area considerably enlarged mucous folds the construction of which is very disordered. On the lesser curvature one can see irregular shapes and a broad niche in a filling defect (fig. 2.). When palpating, the folds seem to be turgescent, hard and tense (fig. 3); they do not disappear nor get deformed. The gastric walls are also tense. The secretion fluid is abundant.

Considering these alarming radiological symptoms, we thought that it was generalized infiltration of the gastric layers, probably of malignant type. Several control X-ray examinations show exactly the same aspects.

Nevertheless, two gastroscopic examinations, made after an interval of a few weeks by two different gastroscopists, fortunately, allow us to cancel the diagnosis of malignant infiltration, and to conclude that it is a giant hypertrophic gastritis.

This latter diagnosis was confirmed by a favorable and very spectacular clinical development obtained from rest, diet and a penicillin treatment. When leaving the hospital (approx. 7 months after the beginning of the gastric episode) the patient has recovered a normal amount of red cells, but there remains a hypochromia (color index: 0.75.).

We have examined this patient again very recently (8 months after he left the hospital). In spite of a very strict medical supervision, he suffers from indefinable dyspeptic troubles and hyposthenia. The X-ray examination of the stomach reveals all symptoms of giant gastritis (fig. 4.). The hematological examination shows: Red cells: 5,400,000, Hemoglobin 86%, color index: 0.8.).

Our second case of hypertrophic gastritis associated with anemia concerns a man of 36 years. In October 1948, he was sent to us for an X-ray examination of the stomach for the following reasons: epigastric pain and diarrheas having lasted for six weeks.

Just before the patient is examined, his diarrheas have stopped, but the pain is persisting; they arrive immediately after meals, are almost unceasing and are not influenced by the food. Moreover, he loses appetite, complains about postprandial meteorism hypersalivation, moderate emaciation and asthenia.

There is nothing special about our patient's antecedents; however, his father is carrier of a rectal carcinoma.

Hereunder are the details of X-ray examinations of this patient (fig. 5 to 8): after passing normally the esophagus, the barium mixture reaches the stomach where there is a small quantity of residual fluid. Then, instead of falling like "snow flakes," as would be the case in simple hypersecretion or stasis on account of pyloric stenosis, the barium runs down the walls very slowly leaving traces which resemble "stearin running down a candle" (Fig. 6).

After the barium has mixed with the residual fluid, a thick mass with small bubbles appears on the surface and remains there during the whole examination. The stiffness of the walls as well as the presence of that vicious liquid make it difficult to cover the internal surface of the stomach (fig. 5 and 6).

After manual massage and compression with an air cushion, it is possible to make appear, on the level

Fig. 5: Giant polypoid gastritis in a case of Biermer's anemia. A male of 36 years; see details in the text. Views of partially filled stomach with broad abdominal compression in vertical position. Note the "moss" appearance.

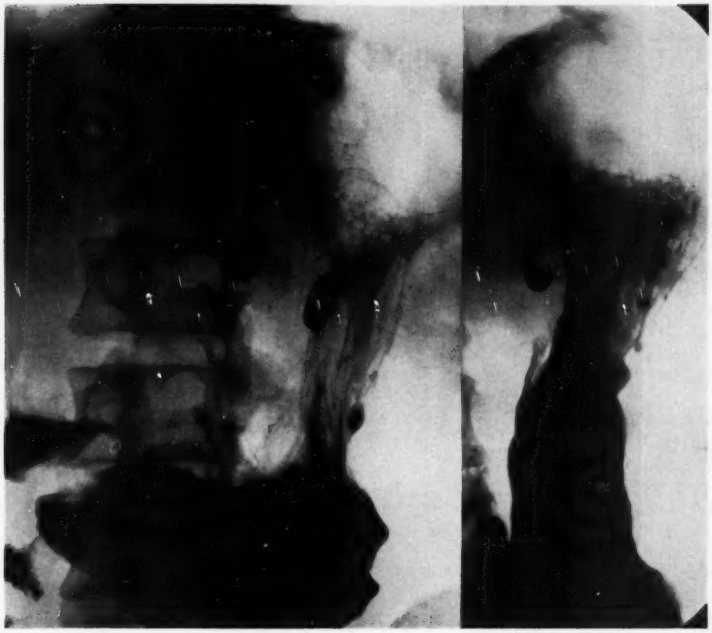

Fig. 6: Same case as fig. 5, six weeks later. Views taken during filling of the stomach in vertical position. Note "moss" and "stearin-running-down-a-candle" appearances.

of the gastric body, extremely enlarged folds having a disordered construction. They are also very turgescent and hardly deformable from palpation. When compressing, the greater curvature of the stomach gives the impression of a pasty mass: deformed from palpation or peristaltic waves, it gets back to its initial shape very slowly.*

The prepylorus and the duodenum are normal.

After complete filling, the affected area of the stomach only shows indentations on the greater curvature, and a few irregular shapes on the lesser curvature.

The peristalsis is very irregular and the evacuation develops rather slowly.

Taking into consideration these radiological observations we have proposed the following diagnosis: giant polypoid gastritis of the gastric body.

However, as it might be a malignant infiltration, we wish to again examine the patient and suggest making a gastroscopy in the meantime.

We wish to point out that in October 1948, the hematological examination was practically normal (red cells: 4,560,000, Hemoglobin 89%, color index: 1). Three radiological control examinations made respectively 10 days, six weeks and nine months later, show the persistence of all elements observed on the first examination. The last examination shows, in addition, an antral spasm and a filling defect of polypoid aspect on the horizontal part of the lesser curvature (fig. 7).

After the second control examination, say approximately six weeks after the first X-ray examination and three months after the clinical beginning of the disease, the practising doctor advised us that several hematological examinations have revealed the evolution of a macrocytic hyperchromic anemia which can be designated as "Biermer's anemia" after having practised the sternal puncture.

In July 1949, a gastroscopy was performed with the following result:

> "Catheterism allows the sucking up a thick and sanguinolent mucus. The antrum seems to be normal.
>
> Through the arcade it is possible to see the pylorus which is normal; on that level, the mucosa is rather pale and without folds. The lesser curvature shows nothing particular but on the greater curvature there appears a broad sanguinolent area with tomentous folds and hypertrophic granulations.
>
> Gastroscopic diagnosis: hemorrhagic giant gastritis."

The patient is treated regularly with hepatic extracts added to vitamin B12 under steady control of his doctor. The clinical and hematological results are satisfactory.

*According to Bücker (1950) this phenomenon happens in extreme cases of plastic gastritis.

Fig. 7: Same case as fig. 5, nine months later. Note the antral spasm and polypoid filling defect.

We have had the opportunity to examine again this patient in March 1951 and in October 1951. He continues his normal professional occupations, does not complain about anything and his anemia is very slight (Red cells: 4,340,000, Hemoglobin 90%, color index 1.04).

Nevertheless, the X-ray examination reveals that all symptoms of giant polypoid gastritis of the gastric body are persisting (fig. 8).

Since October 1948, say three years, the hyperplastic process of the gastric mucosa has neither enlarged nor diminished, in spite of the steady treatment and of a considerable clinical improvement. Only the secretion of mucus has diminished and the antral spasm and polypoid image have disappeared.

Eibach has reported a case of polypoid gastritis which clinically and radiologically has a strange resemblance to the above case: the clinical beginning is identical: epigastric pain, vomiting, diarrhea; the radiological aspects are similar. The changes of the gastric mucosa having been observed for two years and a half remain unchanged. The following difference should however be noted: Eibach's patient is affected by progressive secondary anemia whereas ours has Biermer's anemia.

The clinical observation of our patient and partly of Eibach's patient requires the following comments:

1) The presence of giant polypoid gastritis before the beginning of anemia and its persistence after the clinical healing of the blood disease lead us to believe that the change of the gastric mucosa is the origin but not the consequence of anemia.

2) The abundance of mucous secretion seems to be provocated by an acute outburst of chronic gastritis.

3) The hyperplastic process makes appear changes that could remain irreversible in the layers of the gastric wall.

The future will perhaps reveal if the irreversibility of these apparently benign changes of the gastric mucosa should not be considered as being the beginning of a malignant degeneration. Zdansky's observations concerning this, are very conclusive. He believes, as many others do, that simple hyperplasias of the gastric mucosa, as well as polyposis, lead often to malignant degeneration. Unfortunately, neither radiology nor gastroscopy, nor even inspection and palpation during the operation, allow us to recognize surely the moment of that transformation.

Very recently, we have seen a third case of hyper-

trophic gastritis in a man with hyperchromic macrocytic anemia. The roentgenological appearance is very similar to the former case.

Giant polypoid gastritis can easily be taken for gas-

Fig. 8: Same case as Fig. 5, three years later. The appearance of giant gastritis still persists.

tric polypose or Menetrier's "polyadénomes polypeux." Some authors, such as Konjetzny, Pendergrass, Zdansky and others, believe that chronic gastritis is the beginning of polyposis. Radiologically, the round and neatly demarcated aspect of the clear images arranged in bunches, the flexibility of the gastric wall in the neighborhood of the lesions, and the circumscribed aspect of the affected area will be in favour of polyposis.

We have no personal experience as regards the radiological aspects noticed, exceptionally, in leukemic infiltrations of the stomach.

It results from observations of Desneux, Koch, Lüdin, Pearson and collaborators, Svab, Symmers, Wells and collaborators, that this invasion of the mucosa and the submucosa develops aspects that can be compared with those generally provocated by hypertrophic polypoid gastritis or gastric polyposis ("cerebral convolutions" aspect, according to Pearson).

The differential roentgen diagnosis sets therefore often insolvable problems. The concomitant infiltration of the duodenum, frequent in these cases, is considered as a valuable factor in the differentiation from gastritis (Koch).

We have had the opportunity to observe a case of primitive lymphoma localized in second and third parts of the duodenum. This case made the subject of a special report (Brombart and collaborators) and has enabled us to gather the following radiological signs on a level with the affected parts:

—non uniform dilatation of the duodenum in addition to stasis without stenosis below,

—stiffness of the walls,

—irregularities of outlines,

—filling defects,

—absence of mucous folds.

Our radiological diagnosis was "neoplasic infiltration of the duodenum, probably sarcomatous." The diagnosis after necropsy and histological examination was "primitive malignant lymphoma of the duodenum."

CONCLUSION

The part of the roentgenology is negligible in the diagnosis of the atrophic changes of the gastric mucosa, accompanying anemias.

It is more important in the diagnosis of inflammatory and infiltrating diseases of hypertrophic type.

One should be very careful when interpreting radiological appearances of the gastric mucosa, because its morphological changes may depend upon many functional allergic or pharmacodynamic factors, excluding any inflammation or infiltration.

In case of blood disease, the invariability of the pathological images during repeated radiological examinations has a particular diagnostic value.

The X-ray examination does not allow to recognize the benign kind of a hyperplastic state of gastric mucosa in relation with anemia.

In white cell diseases, the infiltrations of the mucosa and of the deep layers of the stomach, give images similar to those of hypertrophic polypoid gastritis.

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ADRENERGIC BLOCKING AGENTS: THEIR USE IN CLINICAL MEDICINE

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DURING THE past few decades physicians have become accustomed to the fact that there have been only three types of drugs affecting the autonomic nervous system. The first of these was the atropine-like group of drugs, the second was the adrenaline-like drugs, and the third was that which mimicked acetylcholine. These groups of compounds, one depressant and two stimulant in reference to autonomic control, have been used so long that their actions have practically been taken for granted. However, in approaching the last and fourth problem of autonomic control, namely, depressing the adrenergic or sympathetic nervous system, knowledge of the physiology and pharmacology of the sympathetic and parasympathetic nervous system is of prime importance.

It is to be recalled that the autonomic nervous system consists of two main units, namely, the dorso-lumbar or sympathetic division, and the cranio-sacral or parasympathetic division. There are many finely integrated functions of the two divisions of the autonomic nervous system but there are two major features to be considered with respect to the end organs under their control. The first is the gastrointestinal system and its motivation; the parasympathetic division is chiefly excitatory whereas the sympathetic system is largely inhibitory, except at the sphincters where the reverse situation prevails. On the other hand, the sympathetic system is chiefly motoric to the vascular tree, and on stimulation produces vasospasm. Therefore, it follows that since we have two different systems acting antagonistically to each other, they must be in perfect balance for normal function. In alterations of functional control, one may find either over- or underactivity of either system. If overactivity of one division were found, depression of the other division would result. If depression be the original aberration, predominance of the other division would become evident.

Until rather recently we have used the three groups of drugs cited. In cases of parasympathetic overactivity, such as become manifest, e.g., by gastrointestinal spasm, we have relied to a great extent upon atropine and its derivatives or synthetic substitutes. These dampen the transmission of neural impulses across the juncture at the end organ, and thereby diminish, for example, the motoric influence of the parasympathetic outflow, particularly to the gastrointestinal tract. In those cases in which stimulation of the parasympathetics is desirable, as in ileus, bladder atony, etc., such stimulation can be produced by acetylcholine, mecholyl, physostigmine, and others. In regard to the sympathetic outflow, however, therapy in the past has been concerned primarily with stimulating drugs such as adrenaline, ephedrine, benzedrine, cocaine, and others.

It is evident that there is yet a difficult problem in therapy, that of sympathetic predominance. To the pharmacologist, this problem has been that of attempting adrenergic blockade, and during the last few decades numerous possibilities have been studied, but only recently have there been successful attempts in the clinical application of such adrenergic blockade in situations associated with hyperactivity of the sympathetic division. The results of our studies over a four-year period indicate that much more work must be done, but they also offer possibilities of solving many clinical problems, particularly in those patients who come in with a rather vague symptom complex which does not fall into a clearcut category. The concept of autonomic imbalance must be considered and particularly in those patients whose findings indicate the probability of sympathetic predominance.

In order to more clearly understand the mechanism of sympathetic predominance, Figure 1 may offer some assistance.

The outflow of nerve impulses originating in the

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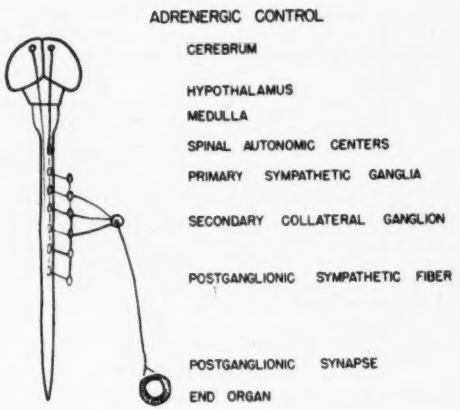

FIG. 1

central axis to the periphery is illustrated: impulses emanating from either the cerebrum, hypothalamus, medulla or spinal autonomic centers may traverse the primary and then the secondary sympathetic ganglia along the sympathetic nerves to the end organ which in this case, let us presume, represents a blood vessel, either superficially located in the skin or in some deeper structure such as the uterine wall. Excitation of impulses along either pathway may result in increased tone of the blood vessel, in other words, the condition of sympathetic predominance. Such vasospasm may manifest itself in any one of the following conditions:

Peripheral vascular disease
- Acrocyanosis
- Acute ischemia (polio)
- Arterio-obliterans
- Causalgias
- Diabetic gangrene
- Dysmenorrhea
- Endarteritis
- Frostbite
- Herpes Zoster
- Livedo reticularis
- Lymphedema
- Popliteal aneurysm and embolism
- Post herpetic neuralgias
- Post traumatic edema
- Raynaud's syndrome
- Scleroderma
- Thrombo-angiitis obliterans
- Thrombophlebitis
- Trench and immersion foot

Cerebral "accidents"
- Thrombotic and vasospastic

Hypertension

In order to release or prevent the vasospasm associated with sympathetic predominance, it is obvious from Figure 1 that there are several points of attack. Barbiturates may conceivably be efficacious because of their sedative action on either the cerebrum, hypothalamus or medulla, and probably also certain portions of the spinal cord, but chiefly on the cerebrum, thus dampening the outflow of excess impulses from the central axis. A direct action of any drug (such as nitrites) upon the blood vessel wall which might produce relaxation of the smooth muscle could also counteract in part the predominant activity of the sympathetic nervous system. Such drugs, however, have not proved too successful in the neurospastic conditions cited above.

Attention was directed early by various investigators toward the possibility of producing a ganglionic blockade at the sympathetic ganglia. The most successful efforts recently produced Etamon (Parke-Davis) which is a long known compound, tetraethylammonium chloride (1). It produces an effective blockade of sympathetic impulses at the synaptic point of transfer from pre- to post-ganglionic fibers, thus throwing a block into the sympathetic system, not at the blood vessel or end organ, but as indicated, higher up in the sympathetic pathways.

A potent adrenergic blocking agent which acts peripherally, i.e., beyond the sympathetic ganglia, is Dibenamine. Its onset of action is slow but prolonged. Unfortunately, it is limited entirely to intravenous administration and is necrotizing if perchance some of the drug be permitted to seep extravascularly. It cannot be given feasibly by the oral route because of its marked irritating action on the gastric mucosa; in this respect it is more limited orally than Etamon. Certain analogues with some advantages have, however, been reported (2).

Certain alkaloids of ergot have been known for their sympathetic blocking capacity as well as their smooth muscle stimulating properties. Ergotoxine, for example, in the experimental animal can very nicely block the effects either of adrenaline administered intravenously or of sympathin (norepinephrine?) produced endogenously by neurofaradization or exogenously administered. In the clinical subject, however, ergotoxine is much too toxic for practical use in most vasospastic conditions. It was therefore interesting to learn of successful attempts of the Sandoz investigators (3) to develop highly effective and less toxic derivatives of the alkaloids contained in the ergotoxine group of ergot alkaloids: Ergocristine, Ergokryptine and Ergocornine.

Another drug capable of producing adrenergic blockade is Priscoline (2-benzyl-imidazoline hydrochloride). A glance at the formula (Figure 2) indicates that it

PRISCOLINE
2-BENZYL-IMIDAZOLINE HYDROCHLORIDE

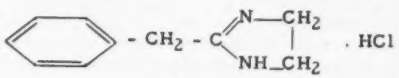

FIGURE 2

is a chemical relative of histamine, the vasodilating properties of which are well known. Apparently, these chemical changes afford a prolonged period of activity. It has been known long on the Continent and in South America but only rather recently has it become available in this country. Evidence of its vasodilating properties can be observed by a flushing or reddening of the skin after its intravenous, intramuscular or oral

administration, and its efficacy has long since been proven in treating vasospasm (4).

In this group of antiadrenergic drugs one finds rather potent vasodilators, and these are very important in treating those peripheral vascular diseases in which vasospasm is a major element; however, in treating hypertension these drugs have been disappointing. Both Etamon and Dibenamine are good hypotensive agents, but they are not practical from the standpoint of office usage because of the route of administration which must be employed. Progress has been made however, in developing drugs which are hypotensive and yet can be given orally and used in office practice. They were discovered in the course of searching for compounds producing adrenergic blockade. One is a peripherally acting drug, Regitine (C-7337) (5) and the other, C-5968, is one which apparently exerts some dampening action on the cerebro-spinal axis (6). Both give promise of being important clinically.

Regitine (C-7337) was studied first. It is not as good as Priscoline as a vasodilator, but it is more hypotensive. The drug has been given to a total of 32 patients, and some of them have been on this therapy for as long as three years. The drug was found to be hypotensive in every case; it has been given orally and all subjects were followed as ambulatory patients. The dose has varied from 75 mg. to 600 mg. daily, given in three or four divided doses. Seven patients are still on the drug and are tolerating it well. Twelve patients were changed to another compound, and thirteen patients have discontinued the drug for various reasons. (Of these thirteen, only two discontinued the drug because of side reactions. Two others became asymptomatic and their blood pressure returned to normal. Some of the others had moved or dropped therapy for personal reasons.)

The following is a summary of the results of Regitine (C-7337) therapy in thirty-two patients:

	Before Regitine	*After Regitine*
B. P. Range	170-260/80-150	120-250/76-128
B. P. Average	224/120	170/102
Average drop in B. P. on Regitine—54 mm. systolic 17 mm. diastolic		

Regitine (C-7337) however, is not without fault. Practically all patients experienced, at one time or other, some degree of tachycardia. This effect could be greatly diminished, however, by initiating therapy with rather small doses (25 mg. t.i.d.) and gradually increasing to the optimum dosage; it is believed now that soon we will be able to control this side reaction in many cases. Another disadvantage of treatment with Regitine is the fact that a certain percentage of the patients developed a tolerance or refractoriness to the drug; actually, this problem is more important than that of tachycardia but it apparently can be successfully handled (7). Of further import is the fact that Regitine can also be used parenterally or orally as an acute agent in hypertensive crises.

The second drug studied for its hypotensive action (8) was C-5968. This compound apparently is a centrally acting drug, probably depressing the sympathetic outflow from the hypothalamus or medulla. It has been given to 18 patients, some of whom have taken the drug for as long as 14 months. There have been no significant mishaps and C-5968 has been found to be hypotensive to a significant degree in every case. The dosage has ranged from 75 mg. to 225 mg. per day, given three to four times daily and all patients are still taking the drug. The following is a summary of the results to date:

	Before C-5958	*After C5968*
B. P. Range	170-260/80-150	140-220/80-120
B. P. Average	229/119	178/97
Average drop in B. P. on C-5968—51 mm. systolic 22 mm. diastolic		

Of the two drugs studied, the patients have stated that C-5968 is "easier to take." The only side reaction encountered so far has been that of headache; this, however, was not too great a problem when the drug was given in gradually increasing doses instead of a full hypotensive dose initially. So far, no evidence of tolerance has been found with C-5968 and no patients have complained of tachycardia.

SUMMARY

In the past one has been able to affect the autonomic nervous system to a varying degree in most respects except in depression of the sympathetic or adrenergic nervous system; but the latter is now becoming a reality in certain respects. The problem of applying adrenergic blockade has been attacked and encouraging results have been obtained so that the medical profession can now treat the varied syndrome of sympathetic predominance. Vasospastic conditions of the vascular tree, including neurogenic or essential hypertension, are peculiarly susceptible in many instances to adrenergic blockade, and it behooves the medical profession to become more aware of the role of sympatholytics and the newer suppressants of sympathetic overflow.

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FAILURE IN THE TREATMENT OF FISTULA-IN-ANO WITH AUREOMYCIN

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FOR SEVERAL hundred years, the accepted treatment for fistula-in-ano has been either fistulotomy, fistulectomy, the seton, or variations and combinations of these methods in one or more stages depending upon the individual case and the choice of the operating surgeon. In complicated cases due to carcinoma, tuberculosis, syphilis, lymphopathia venereum, or ameba, the procedures have been more complicated. In peri-anal fistula, complicating ulcerative colitis, the results of surgery have been very disappointing. Not only have the operated fistulae failed to heal, but the cases have often been severely aggravated to the detriment of the patient's very life. Two cases are herewith presented in which aureomycin therapy was attempted locally:

Case No. 1. A. W. age 44 appeared for office treatment on April 20, 1951 with a history of ulcerative colitis of at least 7 years duration. He had been hospitalized by another physician on two occasions. He was complaining of frequent bloody bowel movements numbering approximately 12 each day. Considerable bloody mucus was passed between movements. On anoscopic and rectoscopic examination, a hypertrophic mucous membrane with multiple polypoid lesions was noted. The mucous membrane was covered with bloody mucus. The polypi were rather firm and irregular on palpation and a biopsy was taken from one of the polyps. The following pathological report was returned on the biopsy:

Gross Examination:

Specimen consists of three minute polypoid structures ranging in size up to 3 mm. in diameter, covered by a brownish mucosa. Consistency is soft. Cut surface is gray-brown. (Entire specimen imbedded.)

Microscopic Examination:

Sections show small polypoid structures, covered by hyperplastic, but regular rectal mucosa. The glands are moderately increased in number and its lumina are frequently filled with a leucocytic exudate. The stroma is heavily infiltrated with all types of inflammatory cells displaying large numbers of eosinophilic leucocytes. There are focal hemorrhages. The surface of all structures is covered by a single layer of uniform, tall columnar epithelium.

Diagnosis:

Multiple actively chronically inflamed, hyperplastic, rectal polyps.

Report from Mt. Sinai Hospital Laboratory dated May 8, 1951.

The patient was placed on cod liver oil, di-calcium phosphate, and vitamin B-12. Marked improvement in the ulcerative colitis occurred. On May 18, 1951, a fistula-in-ano with two openings in the skin of the right anterior peri anal quadrant was noted. The seriousness of this complication and the poor results ordinarily obtained from surgery were weighed and the patient was advised to give the following treatment a trial. Each night a 250 milligram capsule of aureomycin (perforated on each end with a pin) was inserted into the rectum. After six capsules were used in this manner in succession, the patient was advised to return for observation. The previous treatment for the ulcerative colitis was continued. Amazingly enough, after six capsules of aureomycin had been used, pink healthy granulations appeared in both of the external fistulous openings. The colitis continued to improve. Six more capsules of aureomycin were prescribed. After the second series of six capsules were used, one external opening was completely closed and the second was filled with fresh granulations. A third series of six capsules was prescribed. However, no further progress in healing developed and the fistula continued to drain in spite of continued use of the aureomycin capsules in the rectum. The colitis remained under control.

Other pertinent findings on physical examination in case No. 1 were:

Temperature 99, Pulse 84, and Blood Pressure 116/76.

Urinalysis: specific gravity 1.024, acid reaction, albumen and sugar negative, and microscopically negative.

Mouth: teeth—pyorrhea present, tonsils out.

Neck: negative to physical examination.

Heart and Lungs: negative to physical examination.

Abdomen: slight tenderness in left lower quadrant.

Case No. 2. L. W. age 52, a white male appeared for office examination on June 5, 1951. He complained of pain and blood tinged rectal discharge of one month's duration. On examination a fistula-in-ano was found in the right anterior anal quadrant. The patient desired to delay surgery, so the aureomycin therapy was thought worthy of trial. He was instructed to insert one 250 milligram capsule of aureomycin, which had been perforated at each end, nightly for six nights. On June 13, 1951, he reported for an examination and the fistula was found to be completely healed. However, the peri-anal skin showed some evidence of mild pruritic irritation and the patient was advised to limit carbohydrate intake—in spite of a negative sugar on urinalysis. The patient was advised to try another series of six aureomycin capsule rectal insertions. However, after one month the fistula recurred and the patient was operated on September 25, 1951.

Submitted November 6, 1951.

SUMMARY

A new treatment for fistula-in-ano was tried in a case complicated by ulcerative colitis and in an uncomplicated case. A 250 milligram capsule of aureomycin was perforated at both ends and inserted into the rectum each night. The fistulae showed signs of healing in both cases, but later recurred.

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INTESTINAL INTUBATION FOR BARIUM PRODUCED BOWEL OBSTRUCTION

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BARIUM SULPHATE suspension used as a contrast medium to diagnose lesions of the gastrointestinal tract has been developed to the point at which radiologists are able to diagnose even very small lesions. Its use in the diagnosis of bowel obstruction is generally limited to barium enema studies to delineate the bowel distal to an obstructing lesion. It was realized very early that to use barium sulphate for visualization of the upper gastrointestinal tract in the presence of partial or complete bowel obstruction would be extremely dangerous for the patient. The putty-like barium resulting after absorption of the water from the barium sulphate suspensions could effectively plug-up an obstructed bowel as well as causing a partial obstruction to become complete. No radiologist would knowingly use barium sulphate suspension in the routine upper gastrointestinal series if a partial or complete obstruction of the bowel were suspected. Such upper gastrointestinal studies can be carried out even in the presence of partial or complete bowel obstruction if a long intestinal decompression tube is first passed far down into the small bowel (1, 2). The injection of a dilute suspension of barium sulphate through the long intestinal tube safely permits gastrointestinal study. A puddling of the barium will invariably occur at the site of a partial obstruction. A complete blockage of the barium occurs at the site of complete obstruction. After radiological as well as fluoroscopic study of the progress of this barium suspension has been made, and a diagnosis of an obstructing lesion verified, the excess barium sulphate suspension may safely be aspirated by the long intestinal decompression tube.

Despite the universal acceptance of the dictum that barium sulphate suspension must not be given for an upper gastrointestinal series if obstruction of the bowel is suspected, such barium suspensions may be administered because of a failure to diagnose or even suspect the presence of a partial bowel obstruction. The complete obstruction which invariably resulted would then be extremely difficult to correct. Not infrequently the barium remaining after routine upper gastrointestinal series might produce bowel obstruction some days after the radiological study (3, 4, 5, 6).

The use of a long intestinal decompression tube with an 18 fr. lumen (Cantor tube) provides an ideal instrument to remove barium sulphate suspensions given by error in the type of case mentioned. In the case report to be presented, an upper gastrointestinal series was ordered because of a failure to recognize the presence of a partial bowel obstruction. The radiologist noted a greatly distended barium visualized small bowel due to a complete bowel obstruction (see figure 1). This was the result of the barium sulphate suspension converting an incomplete obstruction into a complete one.

Grace Hospital, Detroit.

The same effect has been reported by the too forcible injection of barium sulphate as an enema in the diagnosis of obstructing lesions of the rectosigmoid (7). In cases of this type, the barium sulphate may be forced through incomplete obstructions of the rectosigmoid or sigmoid only to form putty-like masses proximal to the stenosing lesions. A complete obstruction would then result.

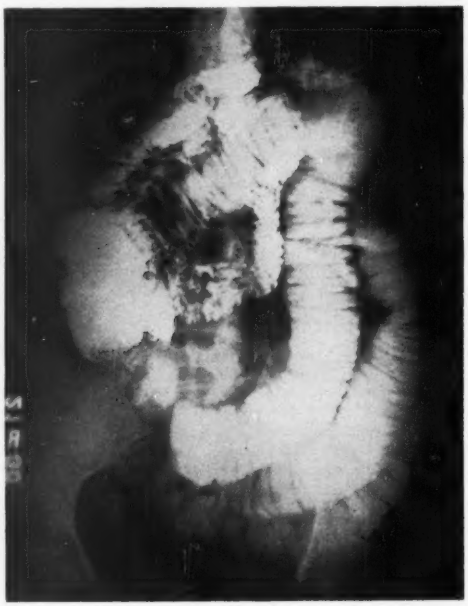

Figure 1: X-ray taken 1-11-49. Note the distension of the small bowel as brought out by the contrast medium.

The treatment of such barium induced bowel obstructions generally consisted in giving large amounts of mineral oil by mouth in an effort to soften the barium mass, kneading of the mass of barium through the intact abdominal wall, high colonic irrigations, and proctoscopic dislodgement with removal of such masses in the pelvic colon. Fatal cases of ileus as a result of barium impaction have been reported (3). Baronofsky found it necessary to do a one stage total colectomy with ileosigmoidostomy to remove a carcinoma of the rectosigmoid and correct a barium induced obstruction of the colon. In this case, an incompletely obstructing carcinoma of the rectosigmoid was converted into a complete obstruction of the colon by the forcible in-

jection of barium sulphate proximal to the stenosing lesion.

Using a single lumen simplified intestinal decompression tube to remove barium sulphate suspensions from the small bowel was found to be a simple, safe, and effective procedure. In forty-eight hours, the barium suspension producing small bowel obstruction may be easily diluted and evacuated through the long intestinal decompression tube. The case being reported is an excellent example of the efficiency of this method of treatment.

CASE REPORT

K. H., a sixty-four year old woman was admitted to the Grace Hospital January 9, 1949 with a diagnosis of gallbladder disease. Her chief complaint was upper right quadrant and epigastric pain. She had been comparatively well until September 1948 at which time she had an attack of epigastric pain which was knife-like in character and was more severe in the right upper quadrant. About two weeks before that Christmas, she began to vomit periodically. This was often associated with diarrhea. This latter would invariably relieve her right upper quadrant pain. Olive oil and orange juice relieved her pain somewhat. At times the pain was generalized over the entire abdomen. The vomiting and diarrhea subsided shortly after Christmas of 1948, but the epigastric pain continued. She now noted difficulty in keeping solid food down. The pain increased in severity. For this reason hospitalization was advised.

Past history: Usual childhood diseases. No previous surgery. Marital: para 11. gravida 11. Family history: mother died of biliary disease. Father died of hypertension. Sister died of kidney disease. No history of tuberculosis, carcinoma, diabetes, or epilepsy in family.

On examination the patient was found to be an elderly white woman of about the stated age. Temperature 99, pulse 100, respiration 24. Head, Eyes, Ears, Nose, Throat, Neck, and Chest: no pathology noted. Abdomen: Soft and not distended. No masses. Tenderness and rigidity with spasticity upon palpation noted in the right upper quadrant, and in the epigastric region. Metallic bowel sounds audible in the upper abdomen. Liver, spleen, and kidneys not palpable. No lymphadenopathy. Reflexes normal.

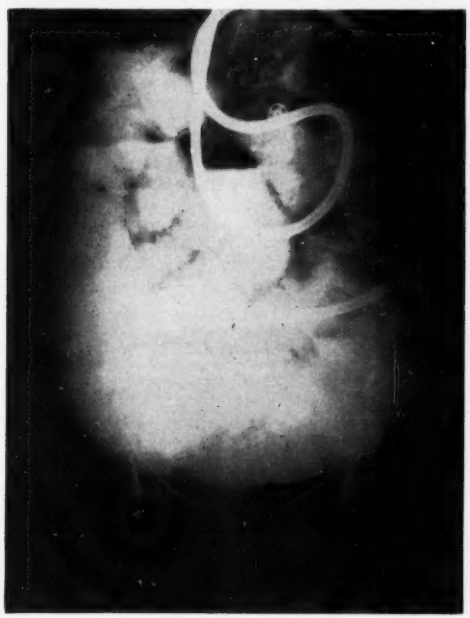

Figure 2: X-ray taken 1-12-49. Note the Cantor tube well down the small bowel in 24 hours.

Laboratory: urine: sp. gr. 1,025, albumin; trace sugar: neg. sediment: negative.

R.B.C. 4,450,000
HHb. 84% 14 grams
W.B.C. 5,400
Polys. 71%
Filaments 65%
Non filaments 6%
Lymphocytes 29%
Kahn: negative

An admission diagnosis of chronic cholecystitis was made.

On January 11, 1949, the patient was given barium sulphate suspension for an upper gastrointestinal series. The following observations were then made:

"No evidence of grossly pathologic conditions could be distinguished on initial fluoroscopic review of the chest and abdomen. On administration of a contrast meal, pronounced so-called curling of the esophagus was observed with retarded passage of contrast fluid through the lumen. The stomach was seen at an unusually high and transverse position. The second duodenal segment descended to a rather low level on the right side so that the duodenal circle appeared somewhat expanded and there also seemed to be some persistent pressure effect on the greater curvature of the gastric antrum from below. Most of the loops of the jejunum filling gradually at this time were seen to the right of the mid-line and ultimately considerable pooling in these loops took place. At the same time, we observed a number of fluid levels in the upper abdomen predominantly to the left of the midline. Suitable roentgenograms were taken of the stomach, duodenum and jejunum. These confirmed our fluoroscopic impressions. The gastroduodenal survey films secured show some intermittent protrusion of prepyloric mucosa into the basal portion of the duodenal bulb. There was some festoon-like looping of the proximal duodenal bend, at times simulating formation of a diverticulum at this level. Subsequent observations covering two hours showed the contrast fluid gradually progressing in the small intestine and diluting markedly with large quantities of retained fluid material in the jejunum and ileum so that ultimately the dilution became so great in the pelvic area and right iliac fossa that it was impossible to distinguish individual loops and the mucosal structure of these intestinal segments. Obviously this patient carries a low obstruction of the small intestine responsible for the observations just recorded.

Diagnosis: Obstruction of the small intestine, in all probability involving a low ileal segment in the right lower abdominal quadrant. Intestinal decompression appears indicated immediately.

Progress. 1-14-49—During the days from 1-11-49 to 1-14-49, an intestinal decompression tube (Cantor) was passed successfully and the bulk of the contrast material removed from the small intestine with a considerable amount of liquid and particulate matter. On these days, 3000 c.c. of liquid was removed from the intestinal tract by the Cantor tube. To remove the barium, it was necessary to irrigate the bowel with 3000 c.c. of water daily in order to keep the barium suspension sufficiently dilute so that it could be aspirated by the Cantor tube. On the days in which this diluting-irrigating process was going on (1-11-49, 1-12-49, and 1-13-49) 6000 c.c. of fluid containing diluted barium, water, and intestinal contents was aspirated daily from the small bowel.

On 1-14-49 radiographic study revealed: "Only minimal amounts of contrast medium seemed to enter the most proximal colonic segments during this period of time. The tip of the Cantor tube was found to be lodged in an unusually low position within the pelvis; that is even caudal to the lower margin of the pubic symphysis so that one might

suspect the obstruction of the small intestine to be located in this area.''

On 1-15-49: Under spinal anaesthesia, a right rectus incision was made. Upon opening the abdomen, the terminal ileum and about 4'' of the cecum and ascending colon showed evidences of acute inflammation. On careful examination a congenital adhesion 4'' from the ileocaecal valve was found to bind the terminal ileum to the posterior peritoneum. This band was cut. It was then noted that the lumen of the bowel was constricted by adhesions reaching from the mesenteric border 2/3 the circumference of the bowel at this point. When these adhesions were all freed, the bowel resumed its normal size. The Cantor tube was left in the bowel just above the point of obstruction and the abdomen closed in layers.

Course: Uneventful recovery. Discharged 1-25-49.

Figure 3: X-ray taken 1-14-49. Note that the barium sulphate as well as the intestinal distension has almost entirely disappeared. 3000 c.c. of intestinal contents were aspirated by means of this tube each day.

SUMMARY

Despite the universal acceptance of the dictum that barium suspension should not be given by mouth to any patient suspected of having intestinal obstruction, an occasional error of this type will occur. This is generally the result of a failure to recognize the presence of a partial obstruction of high degree. In this event, the partial obstruction may be converted into a complete obstruction by the barium contrast medium.

The management of this type of accident is quite simple and effective. A long intestinal decompression tube of adequate caliber should be passed down the gastrointestinal tract. In this type of case because peristaltic activity is generally vigorous in an effort to by-pass the obstructing process, this can usually be rapidly done. The luminal caliber of the long intestinal decompression tube should be as large as possible, preferably 18 fr. With this type of tube well down the bowel, irrigating the bowel through the tube with warm water will effectively dilute the barium suspension permitting its rapid aspiration through the long tube. By this simple method, a serious situation can readily be converted into a relatively simple one. After all the barium has been removed from the bowel and decompression obtained, surgical intervention is indicated to correct the cause of the partial bowel obstruction. In this case reported, a congenital adhesive band was found to be the causative element.

CONCLUSION

1. Intestinal obstruction produced by the unintentional use of barium suspension in a case of partial bowel obstruction, was simply and effectively treated by intubation with a single lumen tube of adequate caliber and holes of sufficiently large size.

2. Surgical intervention is not indicated to remove the barium.

3. Surgical intervention is definitely indicated after proper intestinal decompression in order to correct the obstructing process.

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ESOPHAGEAL HIATUS HERNIA: AN OBSCURE CAUSE OF MASSIVE HEMORRHAGE FROM THE UPPER GASTROINTESTINAL TRACT

LUCIEN W. IDE, M. D. AND JOHN R. McDANIEL, M. D., F. A. C. S., St. Joseph, Mo.

HEMORRHAGE FROM the upper gastrointestinal tract is not commonly attributed to esophageal hiatal hernia in spite of the fact that the literature clearly indicates that the association is not rare (1, 2, 3, 4, 5, 6, 7, 8, 9, 10). Perhaps it is overlooked because it is not considered in the differential diagnosis in hemorrhage from this region or because it may be difficult to demonstrate in some instances by the usual radiological techniques.

A case that was seen recently in the Thompson-Brumm-Knepper Clinic was considered worth reporting because it emphasized the importance of considering hiatal hernia as a cause for massive hemorrhage from the upper gastrointestinal tract and illustrated the value of carefully evaluating the clinical history and findings in the presence of initially normal x-rays and fluoroscopy. Furthermore, it demonstrated the difficulty that can occur in identifying the hernia even when it is strongly suspected.

Case Reports (22, 956) M. R.

A 44 year old white housewife was first seen in the Clinic June 20, 1949, because of epigastric pain commonly radiating to the back, between and under the shoulder blades. It had been particularly troublesome for six months and was usually worse at night often awakening her after three or four hours' sleep. Milk and soda sometimes brought relief, but pork, onions, apples and cucumbers increased the distress. She had passed several black stools and was frequently nauseated but had never vomited.

The sclera, mucous membranes and skin were pale. She weighed 181 pounds and she was 64½ inches tall. The pulse was 82 beats per minute and the blood pressure was 112/80. There were no abnormal heart, lung or abdominal findings excepting moderate generalized abdominal tenderness with muscle spasm in the midepigastrium. There were no rectal or pelvic abnormalities.

There was no albumin or sugar in the urine; the hemoglobin was 7.1 grams per 100 cc. and there were 2,800,000 red blood cells. The white blood count was 3,950 and the Kline exclusion test for syphilis was negative. There was 0.4 mgm. direct and 0.7 mgm. indirect acting serum bilirubin.

X-ray and fluoroscopy of the stomach and duodenum after a barium meal revealed no abnormal findings. (Fig. 1). A barium enema was nonrevealing but there was no dye visualized in the gall-bladder in a cholecystogram after six priodax tablets by mouth. A double dose of the gall bladder dye was repeated four days later and again none was seen in the gall bladder.

Because of the history, nonvisualizing gall bladder in the cholecystogram, and the rather profound anemia, chronic cholecystitis with cholelithiasis and perhaps a carcinoma of the gall bladder were suspected. The patient was hospitalized on July 8, 1949, and after adequate preparation, which included blood transfusions, an exploratory laparotomy and a cholecystectomy were done. Other than moderate scarring and thickening of the gall bladder, no abnormalities were found.

The assistance of Miss Maryan L. Carlson, R.R.L. for helping in collecting and arranging material for this paper is gratefully acknowledged.

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She was discharged on July 18, 1949, free of symptoms but without explanation for her anemia.

The patient was next seen June 30, 1950, when she returned to the Clinic because of recurrent pain similar to the previous distress, which had appeared two weeks before. She had had one attack four months previously lasting two or three days, but otherwise there had been no symptoms since her cholecystectomy. There was a questionable history of jaundice with the previous episode.

She weighed 180 pounds, there was no visible jaundice but there was moderate tenderness in the right upper quadrant of the abdomen. There were 12.7 grams of hemoglobin, 5,300,000 red blood cells and 7,200 white blood cells. There was no direct acting bilirubin detectable but there were 0.5 mg. of the indirect acting type.

On July 3, 1950, after a barium meal, fluoroscopy and x-ray of the stomach, which included examination in the supine position, revealed no hiatal hernia or other abnormality. No shadow casting calculi were seen in the region of the biliary tract.

Five days later the patient went directly to the hospital indicating that her epigastric distress had become worse. Forty-eight hours previous to this admission she had taken an enema for relief of her distress and had passed a large black stool. The day before this admission a large quantity of coffee ground appearing material had been vomited and she had felt too faint to sit up but she had not lost consciousness. Epigastric cramping had become constant, and weakness and palpitation were profound.

Her blood pressure was 100/70. The pulse was 100 per minute. There was marked pallor and the skin was moist and cold. The mid and left portions of the epigastrium were tender and there were black feces in the rectum.

There were 5.2 grams of hemoglobin and 1,620,000 red blood cells. Hemolysis of the red blood cells began at .44 per cent of saline and was complete at .32 per cent. Retraction of the blood clot was complete in 24 hours. Prothrombin determination was 16.7 seconds or 72 per cent of the control.

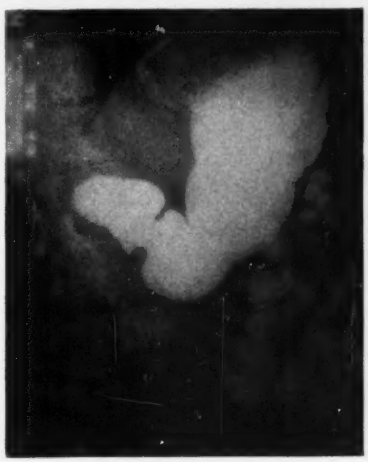

Figure 1: No demonstrable esophageal hiatus hernia in upright position.

There was a negative direct and indirect Van den Bergh reaction and a nonprotein nitrogen of 35.3 mgms. The CO_2 volume per cent was 46 and the blood platelets were 100,000.

She was given supportive care which included 6 pints of whole blood over a period of six days, at the end of which time her hemoglobin was 11.5 grams, her red blood cell count was 3,700,000 and there were no signs of bleeding.

In view of the sequence of events, an attempt was made to elucidate more details in her history. It was found that her symptoms actually dated from 11 or 12 years before. Epigastric bloating had awakened her commonly at night after three or four hours of sleep. She consistently got relief by getting out of bed and walking about after which sleep was usually possible. Daytime distress was sometimes relieved by soda or a glass of milk, but these measures did not give as complete relief as an upright position. Marked relief from her distress was produced by elevating the head of the bed with 12-inch floor blocks.

On July 17, 1950 a qualified hospital radiologist was asked to give the patient a barium meal and x-ray and fluoroscope the stomach with special attention to the possibility of a hiatal hernia. No hiatal herniation was found with a technique which included swallowing barium in a supine position (Fig. 2).

On July 20, 1950, it was asked that the examination be repeated with barium being swallowed in the Trendelenburg position. An esophageal hiatal hernia was demonstrated for the first time (Fig. 3).

OPERATION

The hernia was repaired on July 26, 1950, with a transthoracic approach through the left pleural cavity. It proved to be the more common pulsion type in which the cardiac end of the stomach was pushed upward through the relaxed esophageal hiatus. The esophagus was of normal length. The part of the stomach occupying the sac above the diaphragm measured approximately 5 centimeters in diameter. No evidence of ulceration could be seen or palpated in the stomach wall adjacent to the margins of the hernial ring. When the sac was opened the stomach and duodenum could be explored in their entirety, no source of bleeding was evident. Repair of the hernia was accomplished by excising the sac, placing the protruding portion of the stomach below the diaphragm and reconstructing the hiatus by approximating the diaphragmatic crura anteriorly and posteriorly to the esophagus leaving an adequate opening for the latter.

The patient was given water to drink on the second postoperative day. Diet was gradually increased until she was taking the ordinary foods by the end of a week. She was discharged from the hospital ten days after operation. No difficulty in swallowing has been experienced since the repair of the hernia and she had no other symptoms.

DISCUSSION

Hemorrhage associated with esophageal hiatal hernia may be due to a gastric ulcer or an erosion in the thoracic pouch, an associated esophagitis, or congestion resulting from constriction of the pouch (8). Traumatic ulcers in the lower end of the esophagus close to its junction with the stomach have been attributed to a to-and-fro action of the stomach in the hernial ring when the hernia is small as well as from forceful pressure exerted on the large distorted and congested stomach during the attacks of vomiting when the hernia is large. There is also the additional factor of regurgitation of gastric juices into the lower end of the esophagus which produces esophagitis (9).

Identification of diaphragmatic hernia in consecutive routine gastrointestinal roentgenological examination is fairly common (11). The incidence of hemorrhage varies in different series from 2.5 per cent (1) to 40 per cent (5).

Hiatal hernia has been well named "the masquerader of the upper abdomen" because its symptoms so frequently simulate those of other diseases (12). In a study of 343 cases operated on by Harrington an average of three previous erroneous clinical diagnoses had been made before the correct diagnosis was established (9). In the present case it is evident that the gall bladder that was removed was not responsible for the patient's symptoms, nor did exploration at the time

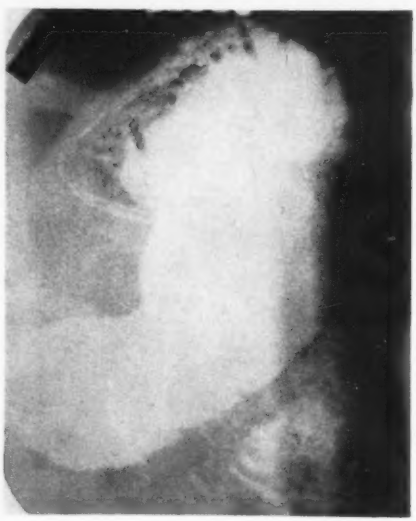

Figure 2: No demonstrable esophageal hiatus hernia in supine position.

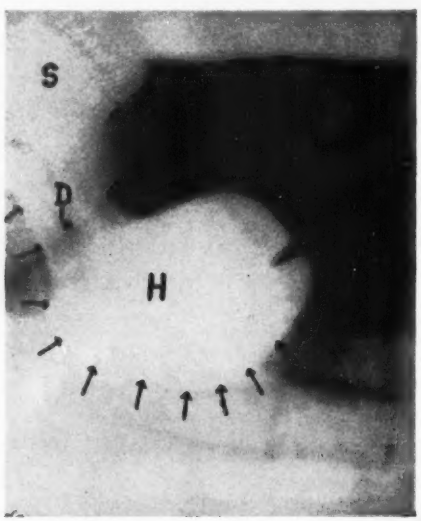

Figure 3: Esophageal hiatus hernia demonstrated in Trendelenburg's position. "H"—herniated stomach. "D"—diaphragm. "S"—stomach.

of cholecystectomy by competent surgeons reveal the true nature of events.

The symptoms may vary from none at all to severe disabling distress. Symptoms may not be characteristic but careful questioning may elicit a fairly characteristic pattern. The symptom complex found to be the most helpful from a diagnostic standpoint is epigastric pain aggravated by reclining or exertion (13). Aggravation by reclining and relief by assuming an upright position was evident in the present instance; and with associated upper gastrointestinal hemorrhage, hiatal hernia was suspected. Shoulder pain from phrenic irritation and pain in the back may accompany other symptoms.

It may be necessary to examine the patient with the head down in a supine position during fluoroscopy and roentgenography to demonstrate hiatal hernia. Various radiological maneuvers for demonstration of hiatal hernias have been well described by Bloom (14). Repeated examinations may be necessary to demonstrate the hernia. The case illustrated pitfalls in establishing the diagnosis radiologically even by qualified radiologists and after the diagnosis was suspected.

Treatment is not necessary in hiatal hernias that do not produce symptoms. Surgery should be reserved for those who have repeated serious bleeding, and those who are disabled by discomfort that is clearly due to hiatal hernia. Occasionally it may be justified when associated conditions cannot be ruled out that demand surgery in themselves.

Conservative measures include a bland diet, antispasmodics such as atropine or tincture of belladonna, and avoiding lying down for two hours after meals. Sleeping with the head of the bed raised with 12-inch floor blocks is a simple measure that may prevent serious discomfort.

If the above forms of treatment do not relieve symptoms and the patient's age and cardiovascular status do not forbid operation, surgical repair of the hernia should be undertaken. Increasing familiarity with the transthoracic approach and the availability of good anesthesia have facilitated exposure and the correction of this condition. Nowadays, the supradiaphragmatic approach is favored by most surgeons because of the wide exposure it offers.

By far the greater number of the hiatus esophageal hernias have the normal length esophagus and repair is accomplished easily by either excising the sac as was done in this case or reducing it by plication followed by reconstructing the abnormally large hiatus. In a few instances the esophagus is abnormally short and the diaphragmatic hiatus will have to be elevated—a not insurmountable problem. In the rare instances this is impossible but relief usually can be afforded by fixing the hiatus securely to the stomach wall.

Morbidity is brief and an adequate dietary intake is possible in a few days. The mortality rate should not exceed 5 per cent.

SUMMARY AND CONCLUSIONS

1. Esophageal hiatal hernia should be considered as a diagnostic possibility in the presence of massive hemorrhage from the upper gastrointestinal tract.

2. Careful evaluation of the history and clinical findings may give the only clue to the correct diagnosis when the fluoroscopy and x-ray are initially normal.

3. Esophageal hiatal hernia may be difficult to demonstrate even when it is suspected.

4. Surgical repair is a necessary and effective measure in the presence of repeated massive hemorrhage.

5. A case is reported illustrating these points, and salient features of the clinical picture and management are discussed.

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ABSTRACTS ON NUTRITION

CALLENDER, S. T. AND LAJTHA, L. G.: *On the nature of Castle's hemopoietic factor.* Blood, VI, 12, Dec. 1951, 1234-1239.

Normal gastric juice (intrinsic factor) and vitamin B_{12} together form a thermolabile hemopoietic factor which ripens megaloblasts in vitro, both gastric juice and B_{12} alone being inactive. The hemopoietic factor in normal serum which ripens megaloblasts in vitro also appears to be thermolabile, heating to 56° C for 2 hours, destroying some of its activity. The results suggest that Castle's original scheme, intrinsic factor plus extrinsic factor equals hemopoietic factor, is still valid today. However, this being true, an interesting problem arises. Crystalline B_{12} given parenterally to persons with pernicious anemia appears in the serum as the active hemopoietic factor, not as free B_{12}. This suggests that in pernicious anemia the intrinsic factor deficiency is only in the gastric juice and there must be an extra-gastric source of intrinsic factor with which the parenterally given B_{12} can combine. This extra-gastric intrinsic factor cannot be present in a free state in the serum, since B_{12} added to pernicious anemia serum has no megaloblastic ripening effect in vitro. Further experiments are planned to investigate the possible source and nature of this factor.

CRONK, G. A.: *Fatigue states associated with abnormal carbohydrate metabolism.* Journal-Lancet, Nov. 1951, 484-487.

Following in the path of the work of Portis and others, Cronk has found that certain fatigue states, due immediately to hypoglycemia, may be benefited by atropine and a high protein, low carbohydrate diet. He also emphasizes that change in occupation and/or psychotherapy may by itself be successful. His blood sugar estimations apparently were seldom if ever carried past the 4th hour, postprandial, and it has been shown by others that sometimes the symptom-producing hypoglycemia may not occur until the 5th or 6th hour. Cronk's article is a good contribution to the large subject of spontaneous hypoglycemia.

CHODOS, R. B. AND ROSS, J. F.: *The effects of combined folic acid and liver extract therapy.* Blood, VI, 12, Dec. 1951, 1213-1233.

Folic acid, when administered alone to persons with pernicious anemia, did not prevent the development or progression of subacute combined degeneration of the spinal cord in 12 of 22 patients receiving this agent for from 12 to 25 months. One patient with total gastrectomy and a macrocytic anemia developed subacute combined degeneration after five months of folic acid treatment. Neurologic disease did not develop in six pernicious anemia patients treated with both folic acid and liver extract for 3½ to 39 months. In ten pernicious anemia patients with good nutrition, neurologic relapses did not progress when liver extract or vitamin B_{12} therapy was instituted, even though folic acid therapy was continued. In two patients with abnormal nutrition and complicating organic abnormalities, nervous system disease progressed after the institution of liver extract therapy.

The authors believe that the hematologic and neurologic manifestations of pernicious anemia (and other macrocytic anemias associated with gastro-intestinal pathology and inadequate nutrition) are due to a deficiency of more than one substance. Folic acid may improve the blood but induce a deficiency of vitamin B_{12} so essential to both blood and nervous system. Such a deficiency will eventually result in a suboptimal blood picture or cord degeneration, or both.

The blood picture in patients with pernicious anemia is not improved by adding folic acid to liver extract or vitamin B_{12} therapy.

HACKEDORN, H. M.: *Some aspects of carbohydrate chemistry.* Bull. Mason Clin., 5, 4, Dec. 1951, 105-111.

Within this century the mechanism by which tissues convert the energy of their food to their own purposes has been evolved. It is a pattern of enzymatic reactions within the cells which progressively releases energy from glucose and other metabolites, converting it into high-energy, organic-phosphate compounds, through the action of adenosine tri-phosphate (A. T. P.). The formation of A. T. P. is efficient only in the presence of oxygen. Members of the B-complex group of vitamins are prosthetic groups for five enzymes of the metabolic cycles. By aid of the enzyme systems one can account for the integration of carbohydrate, lipid and protein metabolism. The energy of A. T. P. is used for muscle contraction, and transmission of nerve impulses, the excretion of urine, reabsorption of glucose and cellular syntheses of all types. The anaerobic phases of carbohydrate metabolism contribute to endochondral bone formation and account for the bacterial production of acids which cause dental caries.

RAKIETEN, M. L., NEWMAN, B., FOLK, K. B. AND MILLER, I.: *Comparison of some constituents in fresh-frozen and freshly-squeezed orange juice.* J. Am. Diabetic Assn., 27, 10, Oct. 1951, 864-868.

Ascorbic acid values for fresh-frozen orange-juice showed a higher average than for freshly-squeezed orange juice. The peel oil concentrations were considerably lower in fresh-frozen than fresh juice. Carbohydrate values showed no difference. In freshly squeezed orange juice the number of bacteria was far greater than in fresh-frozen juice. Coliform organisms in significant numbers were present in fresh juice. None was present in fresh-frozen juice. Hemolytic bacteria were not present in either kind of juice. (The fresh-frozen juice used in this study was Minute Maid, Florida packed).

HINKLE, L. E. AND WOLF, S.: *Importance of life stress in course and management of diabetes mellitus.* J. A. M. A., 148, 7, Feb. 16, 1952, 513-520.

As a result of a 3 year study of eighty diabetics,

experimental evidence indicated that stressful life situations may lead to important metabolic changes, and these changes may be accompanied by emotional changes, and changes in behavior. Under stress, ketonemia and an increased excretion of water, glucose, and chlorides were observed, as well as changes in fasting blood sugar which might lead to either hyper- or hypoglycemia. Developmental, cultural and psychological factors may have an important influence on the onset and course of diabetes. Treatment directed at alteration of the behavior and attitudes of the patient is helpful in abolishing otherwise uncontrollable fluctuations in the course of labile diabetes, and in preventing recurrent episodes of ketosis requiring entry into a hospital.

MEITES, J.: *Changes in nutritional requirements accompanying marked changes in hormone levels.* Metabolism, 1, 1, Jan. 1952, 58-67.

Working with rats, Meites found that marked changes in thyroid, estrogen, or cortisone levels in the body can increase the requirements for B_{12} and possibly other dietary factors. Supplementation of diets with vitamin B_{12} and antibiotics can partially or completely prevent manifestation of dietary deficiencies induced by these hormones. Vitamin B_{12} and the antibiotics do not alter certain characteristic actions of these hormones in the body with the exception that cortisone-induced atrophy of the thymus can be prevented by vitamin B_{12} and aureomycin.

NAKANO, K., HAENO, S., SUGIHARA, S., OKAMOTO, S., OTANI, M. AND KOBAYASHI, S.: *Experimental studies on alloxan diabetes with special reference to hypoglycemia.* Hyogo J. Med. Sci., 1, 1, May 1951.

Carbohydrate concentrations in liver, muscle and brain during the hypoglycemic state due to alloxan, insulin, guanidine and hydrazine and blood sugar determinations were compared. Changes occurring in brain and muscle were always alike. In the liver, alloxan and insulin produced similar results. Also changes due to guanidine and hydrazine were alike. During alloxan or insulin hypoglycemia the liver glycogen changed very little, but a marked decrease was observed in the hypoglycemia caused by guanidine and hydrazine. Guanidine and hydrazine produced much less lowering of blood sugar than insulin or alloxan but the amount of free sugar in the brain decreased more than 50 percent. Hence, hypoglycemic symptoms are probably more related to brain sugar than blood sugar decrease.

WATSON, G. M. AND WITTS, L. J.: *Intestinal macrocytic anemia.* B. M. J., Jan. 5, 1952, 13-17.

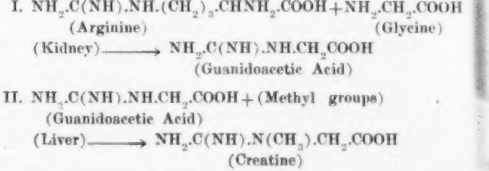
Pernicious anemia may occur in association with intestinal stenosis or anastomoses which permit stagnant loops of gut, and such cases may be cured by surgical correction of the intestinal condition. Experimentally, small intestinal cul-de-sacs were made in the rat and led to macrocytic anemia in a proportion of cases, provided that the cul-de-sac had stagnant contents and was placed in the upper part of the small gut. This anemia was associated with hemolysis and sometimes with steatorrhea. It responded well to folic acid or aureomycin but not at all to vitamin B_{12}.

EDITORIALS

THE RELATIONSHIP BETWEEN ARGININE AND CHOLINE IN CANCER

Several authors, including recently Vrat (1-4) have reported a high arginine content in neoplastic tissue, as well as in regenerating and fetal tissues. Vrat, in addition, found a high arginine content of the blood in these states, especially in cases of carcinoma. We think that Vrat's findings are extremely significant, because his results fit in well with our own work and concepts, using methods entirely different from his (5). We found that in patients with cirrhosis of the liver and in gastro-intestinal and some other carcinomas, if a large test dose of choline is given, it is not utilized and is excreted in the urine. The same test dose of choline given to a normal individual is not excreted, but is utilized presumably in the formation of phospholipid. Wastage of choline is probably associated with a choline deficiency (5a). From our studies, we feel that choline excretion occurs in patients with choline deficiency, probably due to inability to utilize the choline to form phospholipid.

We know that arginine and choline have one link in common. They are both utilized by the body to form creatine, according to the reactions (6):



The first reaction takes place in the kidney and the second takes place in the liver.

In (patients with) cirrhotic livers, methylation is impaired and guanidoacetic acid piles up in the blood and finally is excreted into the urine. Probably this also occurs in carcinoma patients, but this has not been proven.

If in patients with carcinoma, insufficient methyl groups are available for the methylation of guanidoacetic acid, reaction No. I may pile up in the body and thus cause first an increase in guanidoacetic acid and finally an increase in arginine. Presumably this would result in a high arginine content in the blood of the cancer patient. This significant point was made by Vrat.

Vrat (7) also noted that there was a decrease in

arginase activity in neoplastic diseases. Arginase is formed in the liver and catalyzes the hydrolysis of arginine to form ornithine and urea. Vrat (7) has shown that arginase injected in mice bearing spontaneous adenocarcinomas of the breast, caused a reduction in size of the neoplasm and considerable alteration in the histology of the cancer cell. Cytochemical tests showed that the tumor contained no arginine, but contained urea instead. Vrat (8) also noted a similar effect of arginase on the growth of transplanted mammary carcinoma in C_3H mice.

Copeland and his associate (9) produced a chronic choline deficiency in rats by feeding a diet low in choline and methionine but supplemented by minimum doses of choline to prevent death from acute choline deficiency. Cirrhosis of the liver was consistently found in all the rats on the deficient diet. Hepatoma-like neoplasms were found in 10% of the livers. Adenocarcinomas were found in the livers of 30% of the animals. Adenocarcinomas of the lung were found in 38% of the rats. Neoplasms of one or more types were found in 58% of the deficient animals, and no similar lesions were found in litter-mate controls receiving the same diet plus adequate choline supplementation.

Perhaps Copeland's rats had a disturbed arginine-arginase equilibrium as suggested by Vrat's work as a result of choline deficiency. Choline deficiency would not allow for the completion of reaction No. II as cited above, but since reaction No. I is unchecked, it would presumably result in a piling up of guanidoacetic acid and arginine in the tissues and blood. In this manner, arginine excess and choline depletion can be rationalized as separate phases of the same process. Taken in conjunction with our own work on choline excretion in cases of gastro-intestinal cancer (5), it may single out this small area for intensive and concerted research and possible fruitful results.

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A NEW MEDICAL JOURNAL

Grune and Stratton, Inc., who have done such good jobs on "Circulation" and "Blood," now have begun publication of a new journal, "Metabolism." Volume 1, Number 1, January 1952, presents an unusually attractive appearance. Its able Editor is Dr. Samuel Soskin, Michael Reese Hospital, Chicago. The Consulting Editor is Fuller Albright of Boston. All of the Associate Editors are well known and include Ray Farquharson of Toronto and Norman Jolliffe of New York. There is also a sizable list of International Associate Editors. The journal will include in its interest, nutrition, endocrinology, genetics, dystrophies, diabetes and gout. Book reviews and classified abstracts constitute a valuable feature. While some of the contributions are "technical" and deal largely with biochemistry, there are others of a more clinical character. We feel that "Metabolism" is a very valuable addition to the list of American Medical Journals.

MIGRAINE VARIANTS

One meets the occasional patient suffering from recurring attacks of vomiting with or without headache. When the headache is unilateral, a diagnosis of migraine frequently is mandatory although the response to gynergen may vary. Sometimes the headache is of the "tension" type and then the response to ergotamine usually is not striking. In the majority of all these types, x-ray studies of the stomach are non-contributory. Occasionally, during an attack not associated with headache, one finds definite gastric dilatation and, according to Piper (1), these patients may have their attacks aborted by the use of ergotamine. The term "abdominal migraine" has frequently been used, and some authors employ the expression "abdominal epilepsy," apparently because, in a small percentage of cases, minor electroencephalographic abnormalities may appear. It should always be recalled that in *petit mal* as well as *grand mal*, a gastric aura is common. Furthermore, it seems likely that the diagnosis of *diencephalic epilepsy* is commoner than is realized. Particularly in patients whose vomiting attacks are associated with sweating and salivation, it should be considered. Moore (2) has developed this idea extensively.

From a practical standpoint, in many cases where the adult patient experiences recurrent vomiting attacks without headache, gastric abnormality, or the usual signs of either epilepsy or migraine, one can often determine a direct relationship between the attacks and the development of psychic tension. In such cases the use of sedatives may often prove curative of the recurrent vomiting. Finally, although few neurologic textbooks mention it, the symptom of vomiting, as described, is sometimes due to nicotine poisoning and stops soon after tobacco has been given up.

1. Piper, D. W.: Abdominal migraine. Med. J. Australia, Oct. 6, 1951, 468.
2. Moore, M. T.: Abdominal epilepsy. Am. J. Med. Sci., CCXX, 1950, 87.

BOOK REVIEWS

THE PRESENT STATUS OF ANTIBIOTIC THERAPY (with particular reference to Chloramphenicol, Aureomycin and Terramycin). Francis G. Blake, M. D. Charles C. Thomas, Springfield, Ill., 1952, $0.90.

Blake feels that Chloramphenicol, Aureomycin and Terramycin may be substituted for streptomycin in Gram negative infections, and for penicillin in most infections in which penicillin is effective. The book shows the remarkable advance in the treatment of infectious diseases that has been made in the past four years with antibiotic therapy. Each antibiotic is evaluated as to its effectiveness in may unusual as well as the common infections and infestations.

THE BATTLE FOR MENTAL HEALTH. James Clark Moloney, M. D., Philosophical Library, New York, 1952, $3.50.

Almost everyone tends to have his own views with respect to health and disease, in its broadest sense. The present volume contains a theme which is simple enough, but possibly not every physician will adopt it. Moloney believes that artificial bottle feeding in infancy, with consequent comparative lack of close association between mother and infant lies at the base of our increasing national insanity rates. He believes that the "warmly permissive" practices of so-called "primitives" should be adopted by American mothers. The book is worth reading because, whether Moloney is right or wrong, it is a logical contribution to mental hygiene.

ESSENTIALS OF HISTOLOGY. Margaret M. Haskins, Ph. D. and Gerrit Bevelander, Ph. D. The C. V. Mosby Co., St. Louis, 1952, $4.00.

Although a great deal is covered in a space small as compared with "average" texts on histology, this has certain distinct advantages. The most important morphological characteristics of the various tissues are presented in simple and systematic form, and we believe that for the beginner in histology, no better book could be obtained. If the practitioner, long after leaving school, could remember even one-quarter of what is covered here, he would deserve congratulations. We recommend the book not only for beginners but for review purposes.

THE MASTER DICTIONARY OF FOOD AND COOKERY (AND MENU TRANSLATOR). Henry Smith, Philosophical Library, New York, 1952.

This is a book of reference for chefs and all members of the kitchen brigades, for hotel men and caterers. All the various foods and dishes are arranged alphabetically. The book would be somewhat useful to those members of the profession who are gourmets or who make a hobby of cooking, and we understand they constitute about 2 percent of the medical group. The first item under "A," is Aai a la Danube (a famous Austrian dish consisting of eels cooked in wine and served with butter sauce containing chopped hard-cooked eggs) while the last entry under "Z" is Zythos (a beverage made by the ancient Egyptians from wheat, a type of beer, much appreciated by Diodorus). The book contains 263 pages. Smith is a widely-experienced chef and food consultant and the author of several cookery manuals.

GENERAL ABSTRACTS OF CURRENT LITERATURE

SCHWARTZ, L. A.: *Psychodynamic aspects of peptic ulcer.* Harper Hosp. Bull., 9, 3, May-June 1951, 102-110.

Schwartz finds, in a psychological study of ulcer patients, that the early dependency situation is unresolved and poorly managed, with severe distortion of early mother-child relationship. This results in the development of strong passive feminine identification and "retreat from the genital to the oral sadistic (anal) level of libidinous organization."

OLIVEIRA, E. DE, FILHO, P. DE S. C.: *Neurinoma of the rectum.* Rev. Brasil. d. Gastroent., 3, 3, May-June 1951, 275-282.

A successfully operated case of rectal neurinoma is presented and the scant literature on this rare disease is reviewed. The author admits these tumors may become malignant.

GARCIA, M. F., DACOSTA, J. N.: *Prolapse of gastric mucosa.* Rev. Brasil. d. Gastroent., 3, 3, May-June, 1951, 283-304.

Eleven diagnosed cases of prolapse of the gastric mucosa into the duodenum are presented and the literature is reviewed. The condition cannot be diagnosed clinically but only by x-ray. The "open-umbrella" and "mushroom" types are described. All cases present prominent rugae running into or through the pyloric canal. In most cases medical treatment with sedatives, antispasmodics, bland diet, are sufficient. It is wise to avoid emotional tension. The authors recommend the use of antihistaminics.

FLYNN, F. V. AND WALSHE, J. M.: *A study of hepatic function in man before and after partial resection of the liver.* Brit. Med. J., June 30, 1951, 1484-86.

Liver function tests were done before and after

resection of 16 percent of the liver in a case of primary liver cell carcinoma in a non-cirrhotic organ. The serum flocculation tests and the urinary excretion of urobilinogen alone showed changes believed to be attributable to partial resection of the liver. Serum proteins and the pattern of animo acids in the blood and urine showed changes which are believed to be nonspecific in relation to the operation. The following tests failed to register the surgical intervention: plasma prothrombin concentration, blood urea, serum bilirubin, hippuric acid synthesis, bromsulfalein clearance and serum alkaline phosphatase.

MARKSHAK, R. H. AND FRIEDMAN, A. I.: *Carcinoids (argentaffinomas) of the stomach.* Amer. J. Roent. and Rad. Ther., 66, 2, Aug. 1951, 200-203.

Two cases of carcinoids of the stomach are described. Epigastric distress and hematemesis in one case led to x-ray examination which revealed a filling defect on the lesser curvature. At operation this proved to be a carcinoid, 1.7 cm. in diameter. In the other case abdominal distress led to x-ray examination which revealed a filling defect in the pre-pyloric region which, at operation was found to be carcinoid, 1.5 cm. in diameter. In this second case the carcinoid probably was not causing the symptoms, so that its discovery may be regarded as accidental. Carcinoids, except in the appendix, are potentially malignant.

NEILL, D. G.: *Tuberculosis of the liver: a report of five cases.* Med. J. Australia, June 23, 1951, 893-902.

Neill feels that whatever form liver tuberculosis may take (miliary, tuberculomata, or tuberculous cholangitis), it is always secondary, usually to a pulmonary infection, although the primary source may be healed and not in evidence. Absolute diagnosis can only be made by combined histological and bacteriological positive findings on biopsy material. Today, the use of modern drugs makes the possibilities of cure greater than formerly. Liver enlargement may or may not be detectable. Liver function will be affected only where there is very extensive liver involvement.

HALL, W. C.: *Roentgen changes in the upper intestinal tract following the use of calcium chloride in neonatal tetany.* Amer. J. Roent. and Rad. Ther., 66, 2, Aug. 1951, 204-07.

Hall reviews cases indicating that the oral administration of calcium chloride in milk or water to infants suffering from neonatal tetany, although a recognized form of treatment, may lead to serious irritation of the stomach and duodenum with calcification of the visceral wall and ulceration of the mucosa, frequently leading to death. He reports a case in which recovery occurred but in whom a constant constriction of the fundus caused by calcium deposition and later scar formation was noted after 8 months.

RADKE, R. A.: *Treatment of amebiasis with atabrine combined with carbarsone.* Ann. Int. Med., 34, 6, June 1951, 1432-1444.

Radke found atabrine to be an amebacidal agent which is relatively safe to use in the doses recommended. It should be employed in conjunction with another amebacidal agent capable of eliminating the cysts of the organism.

DOIG, R. K., FUNDER, J. F. AND WEIDEN, S.: *Serial gastric biopsy studies in a case of duodenal ulcer treated by deep x-ray therapy.* Med. J. Australia, June 9, 1951, 828-830.

A patient with duodenal ulcer was successfully treated by deep x-ray therapy of the stomach. This is the first report of a study by serial histological and biochemical observations of the complete course of the mucosal reaction to irradiation in the same patient. There was an early and long sustained polymorphonulcear leukocyte infiltration. This lasted almost a year, and then the mesenchymal reaction underwent complete resolution without fibrosis. The gastric acidity and pepsin were greatly depressed for a period of one year. The symptoms of the ulcer disappeared for a year after radiation therapy, although x-ray films showed persistence of deformity in the duodenal cap.

COMFORT, M. W.: *Gastric acidity before and after development of gastric cancer: its etiological, diagnostic and prognostic significance.* Ann. Int. Med., 34, 6, June 1951, 1331-1348.

The degree of subnormality of gastric acidity in gastric cancer varies with sex, age, resectability, symptomatology and size of the cancer. A major part of subnormality of mean gastric secretory activity appears before gastric cancer develops,—even 25 years before. Atrophy of the gastric mucous membrane plays an important role in the depression of gastric secretory activity prior to the development of cancer, and the atrophic gastric mucosa is a soil in which cancer frequently develops. The measurement of free acidity does not enable one to distinguish with certainty between benign and malignant gastric lesions, but it gives valuable information about the relative chances of benignancy and malignancy. The higher the secretory activity of the cancerous stomach, the better are the chances of five year survival.

KIRSCHNER, J. B., PALMER, W. L. AND KLOTZ, A. P.: *Reversibility of ulcerative colitis.* Radiology, 57, 1, July 1951, 1-14.

The course of ulcerative colitis is described in 24 patients, demonstrating the complete clinical reversibility of the disease and the subsidence or pronounced improvement of the x-ray findings. The roentgen evidence of extensive ulcerative colitis disappeared completely in 6 patients. Rectal strictures were no longer demonstrable in two. Patients successfully surviving the initial critical phases of the disease thereafter dealt with recurrences in an increasingly effective manner and ultimately achieved excellent or satisfactory health. ACTH gives promise as a valuable adjunct to treatment.

PETERSON, F. R.: *Surgical diseases of the pancreas.* Miss. Valley Med. J., 73, 4, July 1951, 97-101.

Peterson reviews the surgery of aberrant pancreas, pancreatic cysts, pancreatic calculi, acute pancreatitis, cancer of the pancreas and hyperinsulinism. In the last

disease he insists on Whipple's Triad before operation. After removal of the whole pancreas (where this is necessary) he gives dried extract of the pancreas as well as insulin. He does not mention chronic recurring pancreatitis.

LEMAK, L. L.: *Roentgenological manifestations of gastroduodenal ulceration in the newborn.* Amer. J. Roent. and Rad. Ther., 66, 2, Aug. 1951, 191-199.

Eighteen cases of gastroduodenal ulceration in the newborn were found at Children's Hospital of Michigan, Detroit, and are here presented. Pneumoperitoneum. detected by x-ray, and resulting from perforated ulcers, was the most frequent means of diagnosis, the latter being usually made at autopsy.

LOWE, C. R., OVERY, D. C.: *An evaluation of rigid dietary sodium restriction in the management of ascites in cirrhosis of the liver.* Ann. Int. Med., 34, 6, June 1951, 1396-1403.

Rigid sodium restriction in 8 cases of far-advanced hepatic cirrhosis, along with a diet high in protein and carbohydrate, was found to decrease the amount of ascitic fluid produced, thus sparing the patient considerable protein loss and much discomfort from frequent tapping. However, sodium restriction is not without hazard. If sodium depletion develops, electrolytes should be replaced even if this results in the formation of ascites.

GRAHAM, J.: *Management of gastric ulcer.* Miss. Valley Med. J., 73, 4, July 1951, 101-106.

All instances of gastric ulceration showing persistent achlorhydria should be treated surgically. A lesion diagnosed as gastric ulcer must quickly respond to medical ulcer management or else be subjected to radical surgery. The article points out many of the difficulties encountered in attempting to separate benign from malignant ulcers.

BROWN, C. H. AND SCHNEIDER, R. W.: *Large gastric bezoar.* Cleveland Clin. Quart., 18, 3, July 1951, 203-206.

An unusual case of a phytobezoar caused by ingestion of laundry starch is presented. The x-ray appearance was suggestive of an infiltrative polypoid lesion. Gastroscopy established the diagnosis. Aspiration of the stomach and all night suction with a Levine tube failed to change the appearance of the bezoar on repeated x-ray examinations. Installation of a 1 percent hydrogen peroxide solution and mineral oil, and the subsequent aspiration of the stomach with the large Ewald tube for 4 hours daily on 4 successive days, resulted in the removal of the bezoar.

RICKETTS, W. E.: *Observations on portal cirrhosis with ascites.* Ann. Int. Med., 34, 1, Jan. 1951.

The medical management of patients with or without ascites is similar except for sodium restriction in patients with ascites; the latter procedure controls fluid retention. After several months treatment with high protein, high carbohydrate and high caloric intake, plus additional choline chloride, parenchymal regeneration is favored and plasma albumin rises, thus eliminating edema and ascites. Repeated paracenteses should be avoided since they result in great loss of protein. The ultimate prognosis of patients who have recovered from edema and ascites is determined largely by the incidence of complications, the most frequent of which is bleeding from esophageal varices.

SILVER, H. K.: *Mediterranean anemia in children of non-Mediterranean ancestry.* Am. J. Dis. Child., 80, 5, Nov. 1950.

Silver describes Mediterranean anemia (Cooley's anemia, thalassemia etc.) in 4 families of non-Mediterranean origin, including Chinese, French-Filipino, and Mexican children. The disease is characterized by early onset of progressive anemia, pallor, splenomegaly, mongoloid facies and osteoporosis. The anemia is hypochromic and macrocytic, almost always shows target cells (Mexican hat cells), and the red cells show decreased fragility in hypotonic NaCl solution. The patients are improved by blood transfusions.

IMPROVED BACTERICIDE FOR TOPICAL CHEMOTHERAPY

An improved topical bactericide for use in treatment of ear, nose and throat infections has been introduced nationally by Winthrop-Stearns Inc., according to Dr. Theodore G. Klumpp, president.

Called Sulfamylon Viscous Solution, the preparation affords potent bactericidal action with greatly improved spreading qualities and a longer contact time. It combines 5 per cent Sulfamylon hydrochloride, widely effective germicide and 1 per cent methylcellulose, a thickening agent.

Reporting in Transactions of the American Academy of Ophthalmology and Otolaryngology, of the College of Physicians and Surgeons of Columbia University, Edmund P. Fowler, Jr., M. D., states that he obtained excellent results in a series of 17 patients treated for chronic otitis media or external otitis with Viscous Sulfamylon solution. He noted that the solution was thin enough to allow the patient to instill it into his own external canal, yet thick enough to stick to the sides of the canal to permit a lasting effect. The solution was usually applied after a gentle cleansing of the canal, four times a day, the report said.

Sulfamylon Viscous Solution is recommended for topical chemotherapy wherever a more viscous solution of Sulfamylon is required, especially in the treatment of such localized conditions as upper respiratory infections, ocular infections, otitis media, mastoidectomy and other postoperative cavities.

It is available from Winthrop-Stearns Inc. in bottles of 30 cc. (1 fl. oz.).

ROBINS EXPANDS

E. Claiborne Robins, president of the A. H. Robins Co., Richmond, Va., lifted the first spadeful of ground for the foundation of the pharmaceutical company's new plant on Cummings Drive. Located in a new industrial area of Richmond, it will bring together manufacturing, warehousing and office operations which have outgrown their earlier quarters and are now carried on in separate buildings. The headquarters is scheduled for completion late in the fall of 1952.

ERDWURM NAMED PRESIDENT OF GEORGE A. BREON COMPANY

Graham Erdwurm has been elected president and a director of George A. Breon & Company, pharmaceutical manufacturer, it was announced over the weekend.

Also announced was the election of Dr. Clyde W. Geiter, vice-president and medical director of the Breon Company, to the firm's Board of Directors, and the appointment of Frederick O. S. Spencer as vice-president in charge of sales.

The announcements were made by James Hill, Jr., chairman and president of Sterling Drug Inc., of which the Breon Company is a wholly-owned subsidiary. Breon manufactures medicinal preparations for distribution to dispensing physicians, with plants in Rensselaer, N. Y. and Myerstown, Pa.

Mr. Erdwurm has been associated with Sterling Drug Inc., since January 1947, and has served in various capacities in South Africa, England and the United States. He was born in New York City, the son of a physician. After preparing for the medical profession at Duke and McGill Universities, he joined the staff of the Carnegie Institution as research assistant to Oscar Riddle, PhD., pioneer endocrinologist, and later entered the pharmaceutical industry.

Mr. Erdwurm served in the armed forces during World War II from 1941 to 1946, and attained the rank of Lt. Colonel, Infantry. He served in the European and North African theatres, and was awarded the Legion of Merit.

Dr. Clyde W. Geiter has been associated with the Sterling organization since 1933. He was appointed to the position of medical director of the Breon Company in January 1948, and was elected a vice-president of the firm in November of the same year. In addition to his duties as medical director, Dr. Geiter is in charge of coordinating research in the development of new products, working through the Sterling-Winthrop Research Institute in Rensselaer, N. Y.

A native of Philadelphia, Dr. Geiter earned his Master's degree in pharmacy at the Philadelphia College of Pharmacy in 1926. In 1931, he was graduated from the Creighton College of Medicine, served his internship at the Roxborough Memorial Hospital in Philadelphia, then began medical practice in Detroit.

Mr. Spencer, newly-appointed vice-president in charge of sales for Breon, was born in St. Louis, Mo. Before assuming his new post, he was manager of the retail sales division of Winthrop-Stearns Inc., also a subsidiary of Sterling Drug Inc. He joined the Winthrop organization in 1938, and served from 1941 to 1946 with the U. S. Navy.

He attended Marion Junior College in Kentfield, California and served as instructor of Clinical Chemistry at the Gradwohl School of Laboratory Technique, St. Louis.

MANUSCRIPT EDITING SERVICE ESTABLISHED

To improve medical journalism, the American Medical Writers' Association has recently established the first "Manuscript Editing Service" to be conducted by a medical association in the U. S. For a small fee the Association will edit and criticize medical manuscripts (up to 5,000 words). Its aim is to help authors carry out the dictum of Sydney Smith: "The writer does the most who gives his reader the most knowledge and takes from him the least time." The Association is a non-profit organization with no salaried officers. Its membership includes a large group of well known medical editors and writers. Principal purpose of the group is "to help maintain and advance high standards of medical literature." Further details of the new "Manuscript Editing Service" may be obtained from the Secretary, Harold Swanberg, M. D., 209-224 W. C. U. Building, Quincy, Illinois.

The forthcoming publication of a new international bimonthly is announced by The Nutritional Press of Emmaus, Pa. Called the Journal of Clinical Nutrition it will be devoted to "the practical application of the newer knowledge of nutrition," and will feature original papers, review articles, and an integrated abstract section. The Editorial Board consists of: William Dock, M. D., New York, Grace A.

Goldsmith, M. D., New Orleans, Harold Jeghers, M. D., Chicago, Cyril M. MacBryde, M. D., Saint Louis, M. M. Wintrobe, M. D., Salt Lake City, Michael G. Wohl, M. D., Philadelphia, John B. Youmans, M. D., Nashville, and S. O. Waife. M. D., Philadelphia, Editor-in-Chief. Among the members of the Advisory Board are I. S. Ravdin, M. D., Paul György, M. D., Barnett Sure, Ph. D., H. M. Zimmerman, M. D., Pauline B. Mack, Ph. D., Lester W. Burket, M. D., D. D. S., Charles L. Brown, M. D., and P. H. Belding, D. D. S. Further information bay be obtained from the Journal at 133 South 36th St., Philadelphia 4, Pa.

RONIACOL

Nutley, N. J.—Roniacol Elixir-'Roche' is a new, potent, well-tolerated liquid vasodilator. This palatable elixir provides 50 mg. of Roniacol per teaspoonful in a port wine flavored vehicle. Clinical studies have demonstrated the usefulness of Roniacol in various vasospastic disorders, including some cases of angina pectoris. Richter et al. recently observed (*New York State Journal of Medicine, 51*:1303, 1951) that "Roniacol appears to be more effective as a vasodilator in arteriosclerosis obliterans than other known drugs in common use." Chemically, Roniacol is beta-pyridyl-carbinol (the alcohol corresponding to nicotinic acid).

FIFTH WORLD HEALTH ASSEMBLY TO MEET IN GENEVA MAY 5

Geneva, May 1—The World Health Assembly, legislative organ of the World Health Organization, will hold its fifth regular annual session in Geneva during the three weeks starting on May 5, 1952.

Delegates from most of the 79 member states of the World Health Organization will participate in the Fifth World Health Assembly, as well as representatives of the United Nations and its specialized agencies, and of international technical and welfare organizations.

The business of the Health Assembly will be conducted largely through two main Committees. The *Committee on Programme and Budget* will 1) review the work accomplished by the World Health Organization in 1951 and 2) decide on the programme and budget for 1953, in addition to considering a number of technical matters related to the work of the Organization. The *Committee on Administrative, Financial and Legal Matters* will be concerned with questions of general administration, with constitutional problems, including the admission of new members and associate members, and with staff and financial matters.

For the second successive year a conference-within-a-conference will take place, and the more than 300 delegates expected to attend will be able to participate in informal technical discussions on the following themes: "*The Economic Value of Preventive Medicine*" and: "*Methods of health protection for local areas, as determined by their health, social and economic needs.*"

A three-year grant of $3,500 a year has been made by the A. H. Robins Company, Inc., Richmond, Virginia, to expand a program of clinical research in rheumatic disease at St. Luke's Convalescent Hospital at Greenwich, Connecticut, it is announced by Dr. William R. Bond, Clinical Research Director of the Robins Company.

Clinical results obtained with para-aminobenzoic acid and salicylates (Pabalate,, Robins) will be studied in cases coming through the pediatric and adult medical services of St. Luke's Hospital, New York, and the rheumatic disease service at its convalescent branch in Greenwich.

Results will also be compared with those obtained from treatment with ACTH.

Dr. R. A. Higgons, Director of Convalescent Research, and Dr. Anthony A. Albanese, Chief of Nutritional Research, will head the study.

Numerous clinical observations will be recorded in the cases under study. Laboratory procedures will include determination of blood salicylate levels, amino acid pattern aberrations and their effects on the drug, and electrophoretic patterns of the serum and their modification.

THE AMERICAN CONGRESS OF PHYSICAL MEDICINE

The 30th annual scientific and clinical session of the American Congress of Physical Medicine will be held on August 25, 26, 27, 28 and 29, 1952 inclusive, at The Roosevelt Hotel, New York, N Y. Scientific and clinical sessions will be given on the days of August 25, 26, 27, 28 and 29. All sessions will be open to members of the medical profession in good standing with the American Medical Association. In addition to the scientific sessions, annual instruction seminars will be held. These lectures will be open to physicians as well as to therapists, who are registered with the American Registry of Physical Therapists or the American Occupational Therapy Association. Full information may be obtained by writing to the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Illinois.

A. R. BOSTOCK, 58, BRANCH HOUSE SUPERINTENDENT OF PARKE, DAVIS & COMPANY IN U. S. AND CANADA, IS DEAD

Detroit, March 24—A. R. Bostock, 58, branch house superintendent of Parke, Davis & Company in the United States and Canada, died at Jennings Hospital here today after suffering a heart attack.

Widely-known throughout the pharmaceutical industry, Mr. Bostock had been in charge of improvements and new construction at Parke-Davis' 26 branches in the U. S. and four in Canada since September, 1945. He had entered the hospital March 22 after becoming ill on a business trip to Cincinnati and Atlanta, Ga.

A native of Nuneaton, England, Mr. Bostock came to Detroit when 20 years of age and obtained his first job in the finishing department of Parke, Davis & Company in May, 1913. He was with the pharmaceutical firm more than 38 years.

He became manager of the finishing department, assistant superintendent and then, in 1929, superintendent of stock finishing and traffic. Two years later, the printing and paper box department also was placed under his supervision. His

next promotion was to branch house superindendent.

He was a Mason and a member of the St. Columba Episcopal Church.

Survivors are the widow, Mrs. Nora Bostock, 7732 East Jefferson; a son, Arthur, and a daughter, Mrs. Harold F. McAuley, both of Detroit; and three grandchildren.

Services were held at the Verheyden Funeral Home at 11 a.m. Wednesday, March 26, with burial in Acacia Park Cemetery.

PARKE, DAVIS & COMPANY REDUCES PRICES UP TO 44 PERCENT ON TEN PRODUCTS, INCLUDING PENICILLIN AND STREPTOMYCIN

Detroit, March 27—Parke, Davis & Company, one of the world's oldest and largest pharmaceutical companies, announced late today price reductions on ten different medicinals.

Graydon L. Walker, director of U. S. and Canadian sales, said the decreases, effective at once in both countries, range up to 44 percent on seven different penicillin products.

He added that price cuts of 33 percent have been made on streptomycin and two dihydro-streptomycin products.

The price reductions are the second to be announced by Parke, Davis & Company on high-volume items since Jan. 1, 1952.

TOP EXECUTIVES OF PARKE, DAVIS & CO., MANUFACTURER OF OVER 1,000 DIFFERENT DRUG PRODUCTS, ATTEND NEW ORLEANS MEETING APRIL 3-5

New Orleans—A five-state meeting of approximately 65 salesmen and medical service representatives of Parke, Davis & Company was held here at the Monteleone Hotel April 3, 4 and 5.

A delegation of top executives from the world-wide pharmaceutical firm's home offices in Detroit participated in the discussions on new product developments, market conditions and 1952 sales plans.

They included Graydon L. Walker, director of U. S. and Canadian sales; Dr. E. C. Vonder Heide, associate director of clinical investigation; Frank H. Nelden manager of medical sales education; Walter L. Griffith, manager of professional promotion; H. B. Rames, manager of the chain store sales division; and Merrill W. Dicks, assistant manager of the hospital and biological sales department. Nelden has just returned from a trip to the firm's branches at Mexico City and Colon, Panama, where he established new medical service coverage and training.

Earl A. Kimzey, New Orleans branch manager, presided at the sessions. The branch includes all of Louisiana and part of Alabama, Mississippi, Texas and Florida.

Parke, Davis & Company, which makes more than 1,000 different pharmaceutical products, had net sales of $138,136,475 last year, a 30.7 percent increase over 1950 and a new all-time record.

RADIOISOTOPES BEING STUDIED FOR USE IN CAN MANUFACTURE

American Can Company's research division at Maywood, Ill., is continuing to broaden its research program by investigating the use of radioisotopes—atoms which emit radiation—in tracing complicated chemical and biological processes, the company reported.

O. F. Ecklund, technologist of Canco, is among 32 researchers who attended a four-week course in the techniques of using radioisotopes in research, given at Oak Ridge, Tenn. The course was conducted by the Special Training Division of the Oak Ridge Institute of Nuclear Studies, an educational organization comprising 29 southern universities.

In the company's creative research program, Mr. Ecklund plans to study the use of radioisotopes in food sterilization, for measuring the thickness of metal and organic coatings, and for curing rubber and enamel.

The radioisotope training program at Oak Ridge, which is now in its fourth year, is designed to teach researchers how to use this new scientific tool, which has been called the most important to be developed since the invention of the microscope, it was stated.

A member of the Institute of Food Technology, Mr. Ecklund has wide experience in chemical engineering, and has written a number of publications on the processing of canned foods.

DR. JACKSON

Dr. Eugene L. Jackson, medical director of the A. H. Robins Co., Inc., of Richmond, Va., since 1946, has been elected to a vice-presidency in the company, it was announced by E. Claiborne Robins, president, following a meeting of the board of directors.

The new vice-president will continue his duties as medical director. During the last half decade Dr. Jackson has been in charge of a diversified program of research in connection with the development of such Robins prescription products as *Donnatal Elixir, Pabalate and Robitussin.*

Dr. Jackson was formerly chairman of the department of pharmacology at the Emory University School of Medicine at Atlanta. After an undergraduate major in pharmaceutical chemistry at the University of Michigan, where he was graduated in 1920, Dr. Jackson pursued graduate studies at Michigan, Wisconsin, Emory and Western Reserve Universities. At Western Reserve's Graduate School, he studied with Dr. Torald Sollmann and received his Ph. D. degree in 1939.

Dr. Jackson is a member of the American Association for the advancement of Science, American Society for Pharmacology and Experimental Therapeutics and American Pharmaceutical Association and an affiliate fellow of the American Medical Association. He belongs to Phi Delta Chi, to Sigma Chi, the national honorary scientific fraternity, to Rotary International and the Country Club of Virginia.

Hobbies of the Robins executive include fishing and golf. He was born at French Creek, Ohio. Dr. and Mrs. Jackson now make their home at Malvern Manor, Richmond.

PARKE, DAVIS & COMPANY MAY ESTABLISH NEW PLANTS IN JAPAN AND PHILIPPINES, STOCKHOLDERS LEARN AT ANNUAL MEETING IN DETROIT

Detroit, April 1—Parke, Davis & Company is investigating the possibility of establishing new manufacturing plants in Japan and the Philippines, stockholders learned at their annual meeting here today.

Harry J. Loynd, president, who recently made trips to the Far East

and Latin America, disclosed that two executives would leave in the near future to draw up plans for the expansion in Japan.

"We have decided," he said, "that we must go into Japan not only to protect our business, but to make it possible for the Japanese people to have the benefit of the many life-saving drugs we have to offer.

Loynd said Parke-Davis hoped to be "in a position to manufacture a number of our specialties in Japan in three or four months."

As for the Philippines, Loynd said the decision hadn't yet been made as to whether the firm would take over an existing plant, or build new facilities.

"The Philippines have a terrific future as far as medicine is concerned," he told the stockholders.

Parke, Davis & Company, already one of the world's largest pharmaceutical firms, previously had announced that improvements or new buildings had been completed, are underway, or are being planned for branches in 20 cities in this country and overseas. The plans for Japan and the Philippines had not been revealed until today.

The firm now has overseas branches and laboratories in London, Bombay, Mexico City, Buenos Aires, Havana, Colon (Panama), Rio de Janeiro and Sydney.

PARKE, DAVIS & CO., MAKER OF OVER 1,000 DIFFERENT DRUG PRODUCTS, WILL PAY 45 CENTS A SHARE APRIL 30 AS 258TH CONSECUTIVE DIVIDEND

Detroit, March 31—Parke, Davis & Company directors today declared the pharmaceutical firm's 258th consecutive dividend—a payment of 45 cents a share April 30, 1952, to stockholders of record April 9, 1952.

Maker of more than a thousand different drug products, Parke-Davis has over 22,000 stockholders living in every state and territory, the District of Columbia and virtually all countries this side of the Iron Curtain.

The dividend payment will total more than $2,200,000. As of Dec. 31, 1951, there were 4,896,790 shares outstanding. Last year, Parke-Davis paid a total of $9,298,002 in dividends, an 8.6 percent increase over 1950.

Last month, the firm—one of the oldest and largest of its kind in the world—reported new peaks in both net sales and net earnings for 1951. Net sales rose 30.7 percent to $138,136,475 last year, while net earnings climbed 6.7 percent to $19,053,742 despite materially higher taxes. Parke-Davis has made a profit every year since 1876.

The 85-year-old pharmaceutical firm, whose home offices are in Detroit, now has branches in 26 U. S. and four Canadian cities. There are eight overseas branches, plus numerous direct distributors elsewhere.

PRESCRIBING

Participating in a survey on the practice of substitution in the prescription field, 35 State Boards of Pharmacy, 23 State Pharmaceutical Associations, and a number of organizations allied with the pharma-

ceutical industry have gone on record as being vigorously opposed to this practice.

Comments of these groups represent the preliminary responses to letters of inquiry sent out by E. F. Heffner, Jr., vice-president of the A. H. Robins Co., Inc., of Richmond, Va. Noting that the dispensing of substitute products on prescriptions seemed to be on the increase, Mr. Heffner asked the various groups about their state laws on the subject, and about the stand taken by State Pharmaceutical Associations.

In more than half of the 41 different states which have so far been heard from, there are specific laws forbidding and punishing substitution. Punishment may include fines, suspension, and even revocation of a pharmacist's license or registration certificate. Although in the District of Columbia, Kansas, Nebraska, New Mexico, Oklahoma, Vermont and Virginia there is no specific legislation, state boards and associations have unanimously declared their opposition to substitution, and their desire to cooperate in every possible way to eliminate this practice.

Many of the state associations pointed out that they have been carrying on a continuing program of education against substitution, through repeated mention in their publications, through discussion at meetings, and through resolutions passed at conventions. Considerable interest in the establishment of a suitable program which would effectively discourage substitution has also been held, and a number of proposals to devise a workable plan are under active consideration.

These typical statements, culled from the early survey returns, exemplify the general feeling of all the correspondents:

"A pharmacist who substitutes degrades himself and his profession."

"Our association considers it unethical and unfair competitive business of the lowest type."

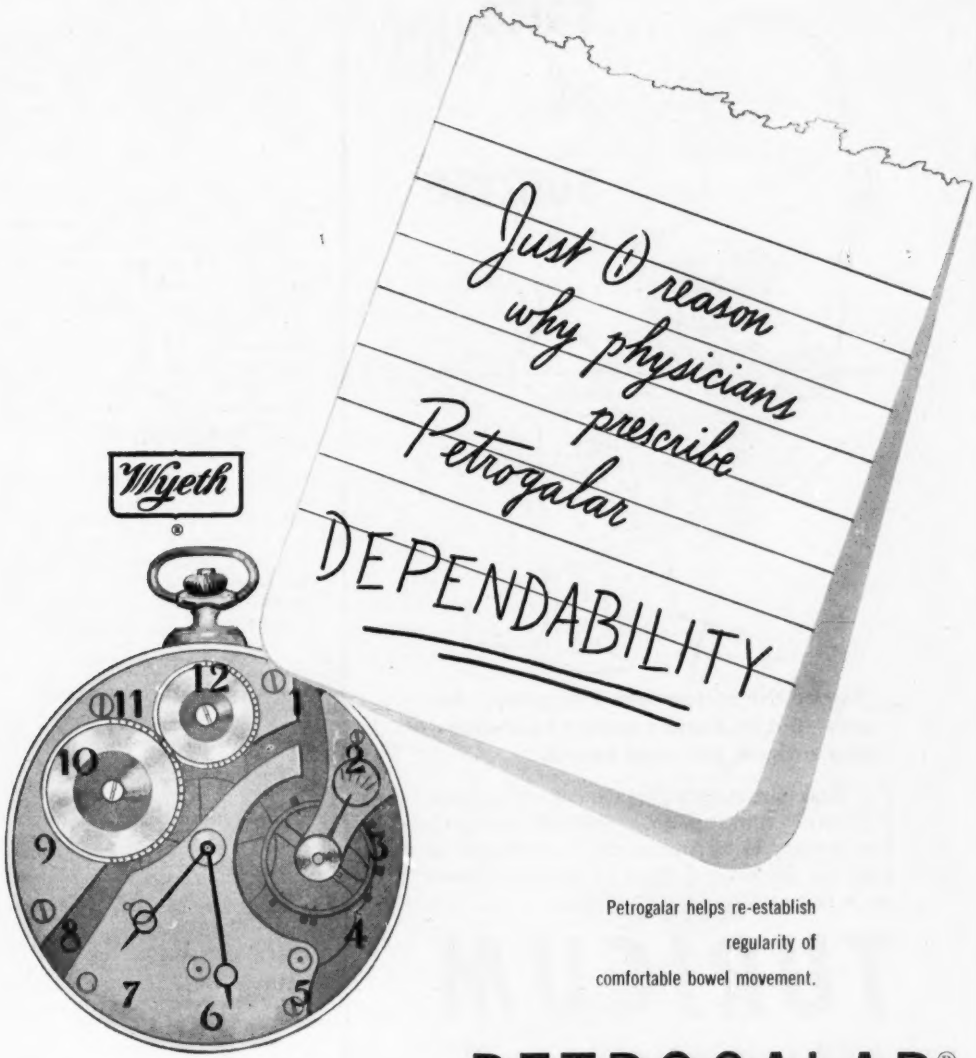
"The ethics of pharmacy demand that a physician's prescription be dispensed as prescribed by the prescriber."

"Our members are decidedly opposed to such a practice for not only does it destroy good will with the members of the medical profession, but it also destroys the professional aspect of pharmacy in the minds of the public."

RETIRED FDA COMMISSIONER HONORED AT CONVENTION

Boca Raton, Fla., April 8—Dr. Paul B. Dunbar, former Commissioner of the Federal Food and Drug Administration, today (Tuesday) received the special annual award of the American Pharmaceutical Manufacturers' Association for outstanding service in helping to uphold the "high standards of public health" in the United States.

The honor was bestowed on Dr. Dunbar at the Association's 45th annual convention being held here at the Boca Raton Club, April 7-9. Making the presentation on behalf of the APMA was Dr. Theodore G. Klumpp, a member of the group's Executive Committee and president of Winthrop-Stearns Inc. Earlier in the day Dr. Rene J. Dubos, world-



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famous authority on tuberculosis, had received the APMA's annual Research Award.

Dr. Dunbar, who retired last year as FDA Commissioner, assumed that post in 1944, succeeding Walter G. Campbell. Both men had worked together in the government agency from the enactment of the first Food and Drugs Act of 1906.

Citing Dr. Dunbar's "firm but fair" policy respecting the certification of food and drug products for public sale, Dr. Klumpp noted that the number of lawsuits against "reputable manufacturers declined during his administration." He attributed to Dr. Dunbar the responsibility for creating "the cooperative feeling and era of good feeling that has existed for some years between the Food and Drug Administration and the industries regulated by it.

"I have always been impressed with the thorough-going honesty of the FDA. From top to bottom there is a solid integrity that runs through the entire organization. The accusing finger of scandal has never been pointed at it, and the chances are it never will," Dr. Klumpp said.

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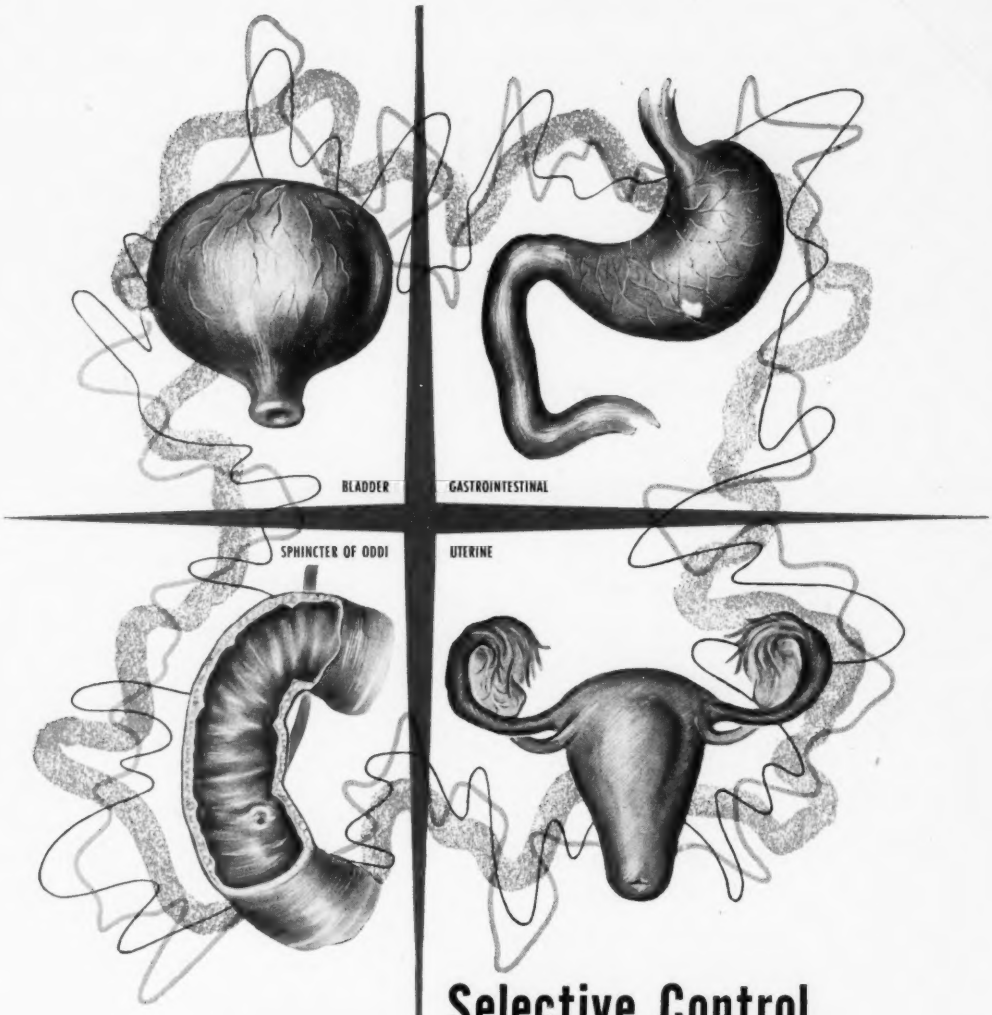

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